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(54) Title: COMPOUNDS AND METHODS FOR THERAPY AND DIAGNOSIS OF LUNG CANCER			
(57) Abstract Compounds and methods for the treatment and diagnosis of lung cancer are provided. The inventive compounds include polypeptides containing at least a portion of a lung tumor protein. Vaccines and pharmaceutical compositions for immunotherapy of lung cancer comprising such polypeptides, or DNA molecules encoding such polypeptides, are also provided, together with DNA molecules for preparing the inventive polypeptides.			

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COMPOUNDS AND METHODS FOR THERAPY AND DIAGNOSIS OF LUNG CANCER

TECHNICAL FIELD

The present invention relates generally to compositions and methods for the treatment and diagnosis of lung cancer. The invention is more specifically related to nucleotide sequences that are preferentially expressed in lung tumor tissue, together with polypeptides encoded by such nucleotide sequences. The inventive nucleotide sequences and polypeptides may be used in vaccines and pharmaceutical compositions for the treatment and diagnosis of lung cancer.

BACKGROUND OF THE INVENTION

Lung cancer is the primary cause of cancer death among both men and women in the U.S., with an estimated 172,000 new cases being reported in 1994. The five-year survival rate among all lung cancer patients, regardless of the stage of disease at diagnosis, is only 13%. This contrasts with a five-year survival rate of 46% among cases detected while the disease is still localized. However, only 16% of lung cancers are discovered before the disease has spread.

Early detection is difficult since clinical symptoms are often not seen until the disease has reached an advanced stage. Currently, diagnosis is aided by the use of chest x-rays, analysis of the type of cells contained in sputum and fiberoptic examination of the bronchial passages. Treatment regimens are determined by the type and stage of the cancer, and include surgery, radiation therapy and/or chemotherapy. In spite of considerable research into therapies for the disease, lung cancer remains difficult to treat.

Accordingly, there remains a need in the art for improved vaccines, treatment methods and diagnostic techniques for lung cancer.

SUMMARY OF THE INVENTION

Briefly stated, the present invention provides compounds and methods for the therapy of lung cancer. In a first aspect, isolated polynucleotide molecules encoding lung

tumor polypeptides are provided, such polynucleotide molecules comprising a nucleotide sequence selected from the group consisting of: (a) sequences provided in SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168 and 171; (b) sequences complementary to a sequence provided in SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168 and 171; and (b) sequences that hybridize to a sequence of (a) or (b) under moderately stringent conditions.

In a second aspect, isolated polypeptides are provided that comprise at least an immunogenic portion of a lung tumor protein or a variant thereof. In specific embodiments, such polypeptides comprise an amino acid sequence encoded by a polynucleotide molecule comprising a nucleotide sequence selected from the group consisting of (a) sequences recited in SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168 and 171; (b) sequences complementary to a sequence provided in SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168 and 171; and (c) sequences that hybridize to a sequence of (a) or (b) under moderately stringent conditions.

In related aspects, expression vectors comprising the inventive polynucleotide molecules, together with host cells transformed or transfected with such expression vectors are provided. In preferred embodiments, the host cells are selected from the group consisting of *E. coli*, yeast and mammalian cells.

In another aspect, fusion proteins comprising a first and a second inventive polypeptide or, alternatively, an inventive polypeptide and a known lung tumor antigen, are provided.

The present invention further provides pharmaceutical compositions comprising one or more of the above polypeptides, fusion proteins or polynucleotide molecules and a physiologically acceptable carrier, together with vaccines comprising one or

more such polypeptides, fusion proteins or polynucleotide molecules in combination with an immune response enhancer.

In related aspects, the present invention provides methods for inhibiting the development of lung cancer in a patient, comprising administering to a patient an effective amount of at least one of the above pharmaceutical compositions and/or vaccines.

Additionally, the present invention provides methods for immunodiagnosis of lung cancer, together with kits for use in such methods. Polypeptides are disclosed which comprise at least an immunogenic portion of a lung tumor protein or a variant of said protein that differs only in conservative substitutions and/or modifications, wherein the lung tumor protein comprises an amino acid sequence encoded by a polynucleotide molecule having a sequence selected from the group consisting of nucleotide sequences recited in SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168 and 171, and variants thereof. Such polypeptides may be usefully employed in the diagnosis and monitoring of lung cancer.

In one specific aspect of the present invention, methods are provided for detecting lung cancer in a patient, comprising: (a) contacting a biological sample obtained from a patient with a binding agent that is capable of binding to one of the above polypeptides; and (b) detecting in the sample a protein or polypeptide that binds to the binding agent. In preferred embodiments, the binding agent is an antibody, most preferably a monoclonal antibody.

In related aspects, methods are provided for monitoring the progression of lung cancer in a patient, comprising: (a) contacting a biological sample obtained from a patient with a binding agent that is capable of binding to one of the above polypeptides; (b) determining in the sample an amount of a protein or polypeptide that binds to the binding agent; (c) repeating steps (a) and (b); and comparing the amounts of polypeptide detected in steps (b) and (c).

Within related aspects, the present invention provides antibodies, preferably monoclonal antibodies, that bind to the inventive polypeptides, as well as diagnostic kits comprising such antibodies, and methods of using such antibodies to inhibit the development of lung cancer.

The present invention further provides methods for detecting lung cancer comprising: (a) obtaining a biological sample from a patient; (b) contacting the sample with a first and a second oligonucleotide primer in a polymerase chain reaction, at least one of the oligonucleotide primers being specific for a polynucleotide molecule that encodes one of the above polypeptides; and (c) detecting in the sample a polynucleotide sequence that amplifies in the presence of the first and second oligonucleotide primers. In a preferred embodiment, at least one of the oligonucleotide primers comprises at least about 10 contiguous nucleotides of a polynucleotide molecule including a sequence selected from the group consisting of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168 and 171.

In a further aspect, the present invention provides a method for detecting lung cancer in a patient comprising: (a) obtaining a biological sample from the patient; (b) contacting the sample with an oligonucleotide probe specific for a polynucleotide molecule that encodes one of the above polypeptides; and (c) detecting in the sample a polynucleotide sequence that hybridizes to the oligonucleotide probe. Preferably, the oligonucleotide probe comprises at least about 15 contiguous nucleotides of a polynucleotide molecule having a partial sequence selected from the group consisting of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168 and 171.

In related aspects, diagnostic kits comprising the above oligonucleotide probes or primers are provided.

In yet a further aspect, methods for the treatment of lung cancer in a patient are provided, the methods comprising obtaining PBMC from the patient, incubating the PBMC with a polypeptide of the present invention (or a polynucleotide that encodes such a polypeptide) to provide incubated T cells and administering the incubated T cells to the patient. The present invention additionally provides methods for the treatment of lung cancer that comprise incubating antigen presenting cells with a polypeptide of the present invention (or a polynucleotide that encodes such a polypeptide) to provide incubated antigen presenting cells and administering the incubated antigen presenting cells to the patient. In certain embodiments, the antigen presenting cells are selected from the group consisting of dendritic cells and macrophages. Compositions for the treatment of lung cancer comprising T cells or antigen presenting cells that have been incubated with a polypeptide or polynucleotide of the

present invention are also provided. These and other aspects of the present invention will become apparent upon reference to the following detailed description. All references disclosed herein are hereby incorporated by reference in their entirety as if each was incorporated individually.

DETAILED DESCRIPTION OF THE INVENTION

As noted above, the present invention is generally directed to compositions and methods for the therapy and diagnosis of lung cancer. The compositions described herein include polypeptides, fusion proteins and polynucleotide molecules. Also included within the present invention are molecules (such as an antibody or fragment thereof) that bind to the inventive polypeptides. Such molecules are referred to herein as "binding agents."

In one aspect, the subject invention discloses polypeptides comprising an immunogenic portion of a human lung tumor protein, wherein the lung tumor protein includes an amino acid sequence encoded by a polynucleotide molecule including a sequence selected from the group consisting of (a) nucleotide sequences recited in SEQ ID NO: 1-109, , 111, 113 115-151, 153, 154,157, 158, 160, 162-164, 167, 168 and 171, (b) the complements of said nucleotide sequences, and (c) variants of such sequences. As used herein, the term "polypeptide" encompasses amino acid chains of any length, including full length proteins, wherein the amino acid residues are linked by covalent peptide bonds. Thus, a polypeptide comprising a portion of one of the above lung tumor proteins may consist entirely of the portion, or the portion may be present within a larger polypeptide that contains additional sequences. The additional sequences may be derived from the native protein or may be heterologous, and such sequences may (but need not) be immunoreactive and/or antigenic. As detailed below, such polypeptides may be isolated from lung tumor tissue or prepared by synthetic or recombinant means.

As used herein, an "immunogenic portion" of a lung tumor protein is a portion that is capable of eliciting an immune response in a patient inflicted with lung cancer and as such binds to antibodies present within sera from a lung cancer patient. Such immunogenic portions generally comprise at least about 5 amino acid residues, more preferably at least about 10, and most preferably at least about 20 amino acid residues. Immunogenic portions of the proteins described herein may be identified in antibody binding assays. Such assays

may generally be performed using any of a variety of means known to those of ordinary skill in the art, as described, for example, in Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, 1988. For example, a polypeptide may be immobilized on a solid support (as described below) and contacted with patient sera to allow binding of antibodies within the sera to the immobilized polypeptide. Unbound sera may then be removed and bound antibodies detected using, for example, ^{125}I -labeled Protein A. Alternatively, a polypeptide may be used to generate monoclonal and polyclonal antibodies for use in detection of the polypeptide in blood or other fluids of lung cancer patients. Methods for preparing and identifying immunogenic portions of antigens of known sequence are well known in the art and include those summarized in Paul, *Fundamental Immunology*, 3rd ed., Raven Press, 1993, pp. 243-247.

The term "polynucleotide(s)," as used herein, means a single or double-stranded polymer of deoxyribonucleotide or ribonucleotide bases and includes DNA and corresponding RNA molecules, including HnRNA and mRNA molecules, both sense and anti-sense strands, and comprehends cDNA, genomic DNA and recombinant DNA, as well as wholly or partially synthesized polynucleotides. An HnRNA molecule contains introns and corresponds to a DNA molecule in a generally one-to-one manner. An mRNA molecule corresponds to an HnRNA and DNA molecule from which the introns have been excised. A polynucleotide may consist of an entire gene, or any portion thereof. Operable anti-sense polynucleotides may comprise a fragment of the corresponding polynucleotide, and the definition of "polynucleotide" therefore includes all such operable anti-sense fragments.

The compositions and methods of the present invention also encompass variants of the above polypeptides and polynucleotides. A polypeptide "variant," as used herein, is a polypeptide that differs from the recited polypeptide only in conservative substitutions and/or modifications, such that the therapeutic, antigenic and/or immunogenic properties of the polypeptide are retained. In a preferred embodiment, variant polypeptides differ from an identified sequence by substitution, deletion or addition of five amino acids or fewer. Such variants may generally be identified by modifying one of the above polypeptide sequences, and evaluating the antigenic properties of the modified polypeptide using, for example, the representative procedures described herein. Polypeptide variants preferably

exhibit at least about 70%, more preferably at least about 90% and most preferably at least about 95% identity (determined as describe below) to the identified polypeptides.

As used herein, a "conservative substitution" is one in which an amino acid is substituted for another amino acid that has similar properties, such that one skilled in the art of peptide chemistry would expect the secondary structure and hydropathic nature of the polypeptide to be substantially unchanged. In general, the following groups of amino acids represent conservative changes: (1) ala, pro, gly, glu, asp, gln, asn, ser, thr; (2) cys, ser, tyr, thr; (3) val, ile, leu, met, ala, phe; (4) lys, arg, his; and (5) phe, tyr, trp, his.

Variants may also, or alternatively, contain other modifications, including the deletion or addition of amino acids that have minimal influence on the antigenic properties, secondary structure and hydropathic nature of the polypeptide. For example, a polypeptide may be conjugated to a signal (or leader) sequence at the N-terminal end of the protein which co-translationally or post-translationally directs transfer of the protein. The polypeptide may also be conjugated to a linker or other sequence for ease of synthesis, purification or identification of the polypeptide (*e.g.*, poly-His), or to enhance binding of the polypeptide to a solid support. For example, a polypeptide may be conjugated to an immunoglobulin Fc region.

A nucleotide "variant" is a sequence that differs from the recited nucleotide sequence in having one or more nucleotide deletions, substitutions or additions. Such modifications may be readily introduced using standard mutagenesis techniques, such as oligonucleotide-directed site-specific mutagenesis as taught, for example, by Adelman et al. (*DNA*, 2:183, 1983). Nucleotide variants may be naturally occurring allelic variants, or non-naturally occurring variants. Variant nucleotide sequences preferably exhibit at least about 70%, more preferably at least about 80% and most preferably at least about 90% identity (determined as described below) to the recited sequence.

The antigens provided by the present invention include variants that are encoded by polynucleotide sequences which are substantially homologous to one or more of the polynucleotide sequences specifically recited herein. "Substantial homology," as used herein, refers to polynucleotide sequences that are capable of hybridizing under moderately stringent conditions. Suitable moderately stringent conditions include prewashing in a

solution of 5X SSC, 0.5% SDS, 1.0 mM EDTA (pH 8.0); hybridizing at 50°C-65°C, 5X SSC, overnight or, in the event of cross-species homology, at 45°C with 0.5X SSC; followed by washing twice at 65°C for 20 minutes with each of 2X, 0.5X and 0.2X SSC containing 0.1% SDS. Such hybridizing polynucleotide sequences are also within the scope of this invention, as are nucleotide sequences that, due to code degeneracy, encode an immunogenic polypeptide that is encoded by a hybridizing polynucleotide sequence.

Two nucleotide or polypeptide sequences are said to be "identical" if the sequence of nucleotides or amino acid residues in the two sequences is the same when aligned for maximum correspondence as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local regions of sequence similarity. A "comparison window" as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, 40 to about 50, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

Optimal alignment of sequences for comparison may be conducted using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins – Matrices for detecting distant relationships. In Dayhoff, M.O. (ed.) *Atlas of Protein Sequence and Structure*, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) Unified Approach to Alignment and Phylogenesis pp. 626-645 *Methods in Enzymology* vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) Fast and sensitive multiple sequence alignments on a microcomputer *CABIOS* 5:151-153; Myers, E.W. and Muller W. (1988) Optimal alignments in linear space *CABIOS* 4:11-17; Robinson, E.D. (1971) *Comb. Theor* 11:105; Santou, N. Nes, M. (1987) The neighbor joining method. A new method for reconstructing phylogenetic trees *Mol. Biol. Evol.* 4:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) *Numerical Taxonomy – the Principles and Practice of Numerical Taxonomy*, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) Rapid similarity searches of nucleic acid and protein data banks *Proc. Natl. Acad. Sci. USA* 80:726-730.

Preferably, the "percentage of sequence identity" is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polynucleotide sequence in the comparison window may comprise additions or deletions (i.e. gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical nucleic acid bases or amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (i.e. the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

Also included in the scope of the present invention are alleles of the genes encoding the nucleotide sequences recited in herein. As used herein, an "allele" or "allelic sequence" is an alternative form of the gene which may result from at least one mutation in the nucleic acid sequence. Alleles may result in altered mRNAs or polypeptides whose structure or function may or may not be altered. Any given gene may have none, one, or many allelic forms. Common mutational changes which give rise to alleles are generally ascribed to natural deletions, additions, or substitutions of nucleotides. Each of these types of changes may occur alone or in combination with the others, one or more times in a given sequence.

For lung tumor polypeptides with immunoreactive properties, variants may, alternatively, be identified by modifying the amino acid sequence of one of the above polypeptides, and evaluating the immunoreactivity of the modified polypeptide. For lung tumor polypeptides useful for the generation of diagnostic binding agents, a variant may be identified by evaluating a modified polypeptide for the ability to generate antibodies that detect the presence or absence of lung cancer. Such modified sequences may be prepared and tested using, for example, the representative procedures described herein.

The lung tumor polypeptides of the present invention, and polynucleotide molecules encoding such polypeptides, may be isolated from lung tumor tissue using any of a variety of methods well known in the art. Polynucleotide sequences corresponding to a gene

(or a portion thereof) encoding one of the inventive lung tumor proteins may be isolated from a lung tumor cDNA library using a subtraction technique as described in detail below. Examples of such polynucleotide sequences are provided in SEQ ID NO: 1-109,111,113 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168 and 171. Partial polynucleotide sequences thus obtained may be used to design oligonucleotide primers for the amplification of full-length polynucleotide sequences from a human genomic DNA library or from a lung tumor cDNA library in a polymerase chain reaction (PCR), using techniques well known in the art (see, for example, Mullis et al., *Cold Spring Harbor Symp. Quant. Biol.* 51:263, 1987; Erlich ed., *PCR Technology*, Stockton Press, NY, 1989). For this approach, sequence-specific primers may be designed based on the nucleotide sequences provided herein and may be purchased or synthesized.

An amplified portion may be used to isolate a full length gene from a suitable library (e.g., a lung tumor cDNA library) using well known techniques. Within such techniques, a library (cDNA or genomic) is screened using one or more polynucleotide probes or primers suitable for amplification. Preferably, a library is size-selected to include larger molecules. Random primed libraries may also be preferred for identifying 5' and upstream regions of genes. Genomic libraries are preferred for obtaining introns and extending 5' sequences.

For hybridization techniques, a partial sequence may be labeled (e.g., by nick-translation or end-labeling with ^{32}P) using well known techniques. A bacterial or bacteriophage library is then screened by hybridizing filters containing denatured bacterial colonies (or lawns containing phage plaques) with the labeled probe (see Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989). Hybridizing colonies or plaques are selected and expanded, and the DNA is isolated for further analysis. cDNA clones may be analyzed to determine the amount of additional sequence by, for example, PCR using a primer from the partial sequence and a primer from the vector. Restriction maps and partial sequences may be generated to identify one or more overlapping clones. The complete sequence may then be determined using standard techniques, which may involve generating a series of deletion clones. The resulting overlapping sequences are then assembled into a single contiguous sequence. A full length

cDNA molecule can be generated by ligating suitable fragments, using well known techniques.

Alternatively, there are numerous amplification techniques for obtaining a full length coding sequence from a partial cDNA sequence. Within such techniques, amplification is generally performed via PCR. Any of a variety of commercially available kits may be used to perform the amplification step. Primers may be designed using techniques well known in the art (*see, for example, Mullis et al., Cold Spring Harbor Symp. Quant. Biol. 51:263, 1987; Erlich ed., PCR Technology, Stockton Press, NY, 1989*), and software well known in the art may also be employed. Primers are preferably 22-30 nucleotides in length, have a GC content of at least 50% and anneal to the target sequence at temperatures of about 68°C to 72°C. The amplified region may be sequenced as described above, and overlapping sequences assembled into a contiguous sequence.

One such amplification technique is inverse PCR (*see Triglia et al., Nucl. Acids Res. 16:8186, 1988*), which uses restriction enzymes to generate a fragment in the known region of the gene. The fragment is then circularized by intramolecular ligation and used as a template for PCR with divergent primers derived from the known region. Within an alternative approach, sequences adjacent to a partial sequence may be retrieved by amplification with a primer to a linker sequence and a primer specific to a known region. The amplified sequences are typically subjected to a second round of amplification with the same linker primer and a second primer specific to the known region. A variation on this procedure, which employs two primers that initiate extension in opposite directions from the known sequence, is described in WO 96/38591. Additional techniques include capture PCR (Lagerstrom et al., *PCR Methods Applic. 1:111-19, 1991*) and walking PCR (Parker et al., *Nucl. Acids. Res. 19:3055-60, 1991*). Transcription-Mediated Amplification, or TMA is another method that may be utilized for the amplification of DNA, rRNA, or mRNA, as described in Patent No. PCT/US91/03184. This autocatalytic and isothermal non-PCR based method utilizes two primers and two enzymes: RNA polymerase and reverse transcriptase. One primer contains a promoter sequence for RNA polymerase. In the first amplification, the promoter-primer hybridizes to the target rRNA at a defined site. Reverse transcriptase creates a DNA copy of the target rRNA by extension from the 3' end of the promoter-primer. The

RNA in the resulting complex is degraded and a second primer binds to the DNA copy. A new strand of DNA is synthesized from the end of the primer by reverse transcriptase creating double stranded DNA. RNA polymerase recognizes the promoter sequence in the DNA template and initiates transcription. Each of the newly synthesized RNA amplicons re-enters the TMA process and serves as a template for a new round of replication leading to the exponential expansion of the RNA amplicon. Other methods employing amplification may also be employed to obtain a full length cDNA sequence.

In certain instances, it is possible to obtain a full length cDNA sequence by analysis of sequences provided in an expressed sequence tag (EST) database, such as that available from GenBank. Searches for overlapping ESTs may generally be performed using well known programs (*e.g.*, NCBI BLAST searches), and such ESTs may be used to generate a contiguous full length sequence.

Once a polynucleotide sequence encoding a polypeptide is obtained, the polypeptide may be produced recombinantly by inserting the polynucleotide sequence into an expression vector and expressing the polypeptide in an appropriate host. Any of a variety of expression vectors known to those of ordinary skill in the art may be employed to express recombinant polypeptides of this invention. Expression may be achieved in any appropriate host cell that has been transformed or transfected with an expression vector containing a polynucleotide molecule that encodes the recombinant polypeptide. Suitable host cells include prokaryotes, yeast, insect and higher eukaryotic cells. Preferably, the host cells employed are *E. coli*, yeast or a mammalian cell line, such as COS or CHO cells. The polynucleotide sequences expressed in this manner may encode naturally occurring polypeptides, portions of naturally occurring polypeptides, or other variants thereof. Supernatants from suitable host/vector systems which secrete the recombinant polypeptide may first be concentrated using a commercially available filter. The concentrate may then be applied to a suitable purification matrix, such as an affinity matrix or ion exchange resin. Finally, one or more reverse phase HPLC steps can be employed to further purify the recombinant polypeptide.

The lung tumor polypeptides disclosed herein may also be generated by synthetic means. In particular, synthetic polypeptides having fewer than about 100 amino

acids, and generally fewer than about 50 amino acids, may be generated using techniques well known to those of ordinary skill in the art. For example, such polypeptides may be synthesized using any of the commercially available solid-phase techniques, such as the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a growing amino acid chain (see, for example, Merrifield, *J. Am. Chem. Soc.* 85:2149-2146, 1963). Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Perkin Elmer/Applied BioSystems Division (Foster City, CA), and may be operated according to the manufacturer's instructions.

In addition, lung tumor antigens may be identified by T cell expression cloning. One source of tumor specific T cells is from surgically excised tumors from human patients. In one method for isolating and characterizing tumor specific T cells, the excised tumor is minced and enzymatically digested for several hours to release tumor cells and infiltrating lymphocytes (tumor infiltrating T cells, or TILs). The cells are washed in HBSS buffer and passed over a Ficoll (100%/75%/HBSS) discontinuous gradient to separate tumor cells and lymphocytes from non-viable cells. Two bands are harvested from the interfaces; the upper band at the 75%/HBSS interface contains predominantly tumor cells, while the lower band at the 100%/75%/HBSS interface contains a majority of lymphocytes. The TILs are expanded in culture by techniques well known in the art, but preferably in culture media supplemented with 10 ng/ml IL-7 and 100 U/ml IL-2, or alternatively, cultured and expanded in tissue culture plates that have been pre-adsorbed with anti-CD3 monoclonal antibody (OKT3). The resulting TIL cultures are analyzed by FACS to confirm that the vast majority are CD8+ T cells (>90% of gated population).

In addition, the tumor cells are also expanded in culture using standard techniques well known in the art to establish a tumor cell line, which is later confirmed to be lung carcinoma cells by immunohistochemical analysis. The tumor cell line is transduced with a retroviral vector to express human CD80. The tumor cell line is further characterized by FACS analysis to confirm the strong expression levels of CD80, class I and II MHC molecules.

The specificity of the TIL lines to lung tumor is confirmed by INF- γ and/or TNF- α cytokine release assays. For example, TIL cells from day 21 cultures are co-cultured

with either autologous or allogeneic tumor cells, EBV-immortalized LCL, or control cell lines Daudi and K562 and the culture supernatant monitored by ELISA for the presence of cytokines. The expression of these specific cytokines in the presence of tumor or negative control cells indicates whether the TIL lines are tumor specific and potentially recognizing tumor antigen presented by the autologous MHC molecules.

The characterized tumor-specific TIL lines can be expanded and cloned by methods well known in the art. For example, the TIL lines may be expanded to suitable numbers for T cell expression cloning by using soluble anti-CD3 antibody in culture with irradiated EBV transformed LCLs and PBL feeder cells in the presence of 20 U/ml IL-2. Clones from the expanded TIL lines can be generated by standard limiting dilution techniques. In particular, TIL cells are seeded at 0.5 cells/well in a 96-well U bottom plate and stimulated with CD-80-transduced autologous tumor cells, EBV transformed LCL, and PBL feeder cells in the presence of 50 U/ml IL-2. These clones may be further analyzed for tumor specificity by ^{51}Cr microcytotoxicity and IFN- γ bioassays. Additionally, the MHC restriction element recognized by the TIL clones may be determined by antibody blocking studies well known in the art.

The CTL lines or clones described above may be employed to identify tumor specific antigens. For example, autologous fibroblasts or LCL from a patient may be transfected or transduced with polynucleotide fragments derived from a lung tumor cDNA library to generate target cells expressing tumor polypeptides. The target cells expressing tumor polypeptides in the context of MHC will be recognized by the CTL line or clone resulting in T-cell activation, which can be monitored by cytokine detection assays. The tumor gene being expressed by the target cell and recognized by the tumor-specific CTL is then isolated by techniques described above. In general, regardless of the method of preparation, the polypeptides disclosed herein are prepared in an isolated, substantially pure form (*i.e.*, the polypeptides are homogenous as determined by amino acid composition and primary sequence analysis). Preferably, the polypeptides are at least about 90% pure, more preferably at least about 95% pure and most preferably at least about 99% pure. In certain preferred embodiments, described in more detail below, the substantially pure polypeptides

are incorporated into pharmaceutical compositions or vaccines for use in one or more of the methods disclosed herein.

In a related aspect, the present invention provides fusion proteins comprising a first and a second inventive polypeptide or, alternatively, a polypeptide of the present invention and a known lung tumor antigen, together with variants of such fusion proteins. The fusion proteins of the present invention may (but need not) include a linker peptide between the first and second polypeptides.

A polynucleotide sequence encoding a fusion protein of the present invention is constructed using known recombinant DNA techniques to assemble separate polynucleotide sequences encoding the first and second polypeptides into an appropriate expression vector. The 3' end of a DNA sequence encoding the first polypeptide is ligated, with or without a peptide linker, to the 5' end of a DNA sequence encoding the second polypeptide so that the reading frames of the sequences are in phase to permit mRNA translation of the two DNA sequences into a single fusion protein that retains the biological activity of both the first and the second polypeptides.

A peptide linker sequence may be employed to separate the first and the second polypeptides by a distance sufficient to ensure that each polypeptide folds into its secondary and tertiary structures. Such a peptide linker sequence is incorporated into the fusion protein using standard techniques well known in the art. Suitable peptide linker sequences may be chosen based on the following factors: (1) their ability to adopt a flexible extended conformation; (2) their inability to adopt a secondary structure that could interact with functional epitopes on the first and second polypeptides; and (3) the lack of hydrophobic or charged residues that might react with the polypeptide functional epitopes. Preferred peptide linker sequences contain Gly, Asn and Ser residues. Other near neutral amino acids, such as Thr and Ala may also be used in the linker sequence. Amino acid sequences which may be usefully employed as linkers include those disclosed in Maratea et al., *Gene* 40:39-46, 1985; Murphy et al., *Proc. Natl. Acad. Sci. USA* 83:8258-8262, 1986; U.S. Patent No. 4,935,233 and U.S. Patent No. 4,751,180. The linker sequence may be from 1 to about 50 amino acids in length. Peptide sequences are not required when the first and second

polypeptides have non-essential N-terminal amino acid regions that can be used to separate the functional domains and prevent steric interference.

The ligated polynucleotide sequences are operably linked to suitable transcriptional or translational regulatory elements. The regulatory elements responsible for expression of polynucleotide are located only 5' to the DNA sequence encoding the first polypeptides. Similarly, stop codons require to end translation and transcription termination signals are only present 3' to the DNA sequence encoding the second polypeptide.

Fusion proteins are also provided that comprise a polypeptide of the present invention together with an unrelated immunogenic protein. Preferably the immunogenic protein is capable of eliciting a recall response. Examples of such proteins include tetanus, tuberculosis and hepatitis proteins (see, for example, Stoute et al. *New Engl. J. Med.*, 336:86-91 (1997)).

Polypeptides of the present invention that comprise an immunogenic portion of a lung tumor protein may generally be used for therapy of lung cancer, wherein the polypeptide stimulates the patient's own immune response to lung tumor cells. The present invention thus provides methods for using one or more of the compounds described herein (which may be polypeptides, polynucleotide molecules or fusion proteins) for immunotherapy of lung cancer in a patient. As used herein, a "patient" refers to any warm-blooded animal, preferably a human. A patient may be afflicted with disease, or may be free of detectable disease. Accordingly, the compounds disclosed herein may be used to treat lung cancer or to inhibit the development of lung cancer. The compounds are preferably administered either prior to or following surgical removal of primary tumors and/or treatment by administration of radiotherapy and conventional chemotherapeutic drugs.

In these aspects, the inventive polypeptide is generally present within a pharmaceutical composition or a vaccine. Pharmaceutical compositions may comprise one or more polypeptides, each of which may contain one or more of the above sequences (or variants thereof), and a physiologically acceptable carrier. The vaccines may comprise one or more such polypeptides and a non-specific immune-response enhancer, wherein the non-specific immune response enhancer is capable of eliciting or enhancing an immune response to an exogenous antigen. Examples of non-specific-immune response enhancers include

adjuvants, biodegradable microspheres (e.g., polylactic galactide) and liposomes (into which the polypeptide is incorporated). Pharmaceutical compositions and vaccines may also contain other epitopes of lung tumor antigens, either incorporated into a fusion protein as described above (i.e., a single polypeptide that contains multiple epitopes) or present within a separate polypeptide.

Alternatively, a pharmaceutical composition or vaccine may contain polynucleotide encoding one or more of the above polypeptides and/or fusion proteins, such that the polypeptide is generated *in situ*. In such pharmaceutical compositions and vaccines, the polynucleotide may be present within any of a variety of delivery systems known to those of ordinary skill in the art, including nucleic acid expression systems, bacteria and viral expression systems. Appropriate nucleic acid expression systems contain the necessary polynucleotide sequences for expression in the patient (such as a suitable promoter). Bacterial delivery systems involve the administration of a bacterium (such as *Bacillus Calmette-Guerrin*) that expresses an epitope of a lung cell antigen on its cell surface. In a preferred embodiment, the polynucleotides may be introduced using a viral expression system (e.g., vaccinia or other pox virus, retrovirus, or adenovirus), which may involve the use of a non-pathogenic (defective), replication competent virus. Suitable systems are disclosed, for example, in Fisher-Hoch et al., *PNAS* 86:317-321, 1989; Flexner et al., *Ann. N.Y. Acad. Sci.* 569:86-103, 1989; Flexner et al., *Vaccine* 8:17-21, 1990; U.S. Patent Nos. 4,603,112, 4,769,330, and 5,017,487; WO 89/01973; U.S. Patent No. 4,777,127; GB 2,200,651; EP 0,345,242; WO 91/02805; Berkner, *Biotechniques* 6:616-627, 1988; Rosenfeld et al., *Science* 252:431-434, 1991; Kolls et al., *PNAS* 91:215-219, 1994; Kass-Eisler et al., *PNAS* 90:11498-11502, 1993; Guzman et al., *Circulation* 88:2838-2848, 1993; and Guzman et al., *Cir. Res.* 73:1202-1207, 1993. Techniques for incorporating polynucleotide into such expression systems are well known to those of ordinary skill in the art. The polynucleotides may also be "naked," as described, for example, in published PCT application WO 90/11092, and Ulmer et al., *Science* 259:1745-1749, 1993, reviewed by Cohen, *Science* 259:1691-1692, 1993. The uptake of naked polynucleotides may be increased by coating the polynucleotides onto biodegradable beads, which are efficiently transported into the cells.

Routes and frequency of administration, as well as dosage, will vary from individual to individual and may parallel those currently being used in immunotherapy of other diseases. In general, the pharmaceutical compositions and vaccines may be administered by injection (e.g., intracutaneous, intramuscular, intravenous or subcutaneous), intranasally (e.g., by aspiration) or orally. Between 1 and 10 doses may be administered over a 3-24 week period. Preferably, 4 doses are administered, at an interval of 3 months, and booster administrations may be given periodically thereafter. Alternate protocols may be appropriate for individual patients. A suitable dose is an amount of polypeptide or polynucleotide that is effective to raise an immune response (cellular and/or humoral) against lung tumor cells in a treated patient. A suitable immune response is at least 10-50% above the basal (i.e., untreated) level. In general, the amount of polypeptide present in a dose (or produced *in situ* by the polynucleotide molecule(s) in a dose) ranges from about 1 pg to about 100 mg per kg of host, typically from about 10 pg to about 1 mg, and preferably from about 100 pg to about 1 µg. Suitable dose sizes will vary with the size of the patient, but will typically range from about 0.01 mL to about 5 mL.

While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier will vary depending on the mode of administration. For parenteral administration, such as subcutaneous injection, the carrier preferably comprises water, saline, alcohol, a lipid, a wax and/or a buffer. For oral administration, any of the above carriers or a solid carrier, such as mannitol, lactose, starch, magnesium stearate, sodium saccharine, talcum, cellulose, glucose, sucrose, and/or magnesium carbonate, may be employed. Biodegradable microspheres (e.g., polylactic glycolide) may also be employed as carriers for the pharmaceutical compositions of this invention. Suitable biodegradable microspheres are disclosed, for example, in U.S. Patent Nos. 4,897,268 and 5,075,109.

Any of a variety of immune-response enhancers may be employed in the vaccines of this invention. For example, an adjuvant may be included. Most adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a nonspecific stimulator of immune response, such as lipid A, *Bordella pertussis* or *Mycobacterium tuberculosis*. Such adjuvants are commercially

available as, for example, Freund's Incomplete Adjuvant and Complete Adjuvant (Difco Laboratories, Detroit, MI) and Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ). Polypeptides and polynucleotides disclosed herein may also be employed in adoptive immunotherapy for the treatment of cancer. Adoptive immunotherapy may be broadly classified into either active or passive immunotherapy. In active immunotherapy, treatment relies on the *in vivo* stimulation of the endogenous host immune system to react against tumors with the administration of immune response-modifying agents (for example, tumor vaccines, bacterial adjuvants, and/or cytokines).

In passive immunotherapy, treatment involves the delivery of biologic reagents with established tumor-immune reactivity (such as effector cells or antibodies) that can directly or indirectly mediate antitumor effects and does not necessarily depend on an intact host immune system. Examples of effector cells include T lymphocytes (for example, CD8+ cytotoxic T-lymphocyte, CD4+ T-helper, gamma/delta T lymphocytes, tumor-infiltrating lymphocytes), killer cells (such as Natural Killer cells, lymphokine-activated killer cells), B cells, or antigen presenting cells (such as dendritic cells and macrophages) expressing the disclosed antigens. The polypeptides disclosed herein may also be used to generate antibodies or anti-idiotypic antibodies (as in U.S. Patent No. 4,918,164), for passive immunotherapy.

The predominant method of procuring adequate numbers of T-cells for adoptive immunotherapy is to grow immune T-cells *in vitro*. Culture conditions for expanding single antigen-specific T-cells to several billion in number with retention of antigen recognition *in vivo* are well known in the art. These *in vitro* culture conditions typically utilize intermittent stimulation with antigen, often in the presence of cytokines, such as IL-2, and non-dividing feeder cells. As noted above, the immunoreactive polypeptides described herein may be used to rapidly expand antigen-specific T cell cultures in order to generate sufficient number of cells for immunotherapy. In particular, antigen-presenting cells, such as dendritic, macrophage, monocyte, fibroblast, or B-cells, may be pulsed with immunoreactive polypeptides, or polynucleotide sequence(s) may be introduced into antigen presenting cells, using a variety of standard techniques well known in the art. For example, antigen presenting cells may be transfected or transduced with a polynucleotide sequence,

wherein said sequence contains a promoter region appropriate for increasing expression, and can be expressed as part of a recombinant virus or other expression system. Several viral vectors may be used to transduce an antigen presenting cell, including pox virus, vaccinia virus, and adenovirus; also, antigen presenting cells may be transfected with polynucleotide sequences disclosed herein by a variety of means, including gene-gun technology, lipid-mediated delivery, electroporation, osmotic shock, and particulate delivery mechanisms, resulting in efficient and acceptable expression levels as determined by one of ordinary skill in the art. For cultured T-cells to be effective in therapy, the cultured T-cells must be able to grow and distribute widely and to survive long term *in vivo*. Studies have demonstrated that cultured T-cells can be induced to grow *in vivo* and to survive long term in substantial numbers by repeated stimulation with antigen supplemented with IL-2 (see, for example, Cheever, M., *et al*, "Therapy With Cultured T Cells: Principles Revisited," *Immunological Reviews*, 157:177, 1997).

The polypeptides disclosed herein may also be employed to generate and/or isolate tumor-reactive T-cells, which can then be administered to the patient. In one technique, antigen-specific T-cell lines may be generated by *in vivo* immunization with short peptides corresponding to immunogenic portions of the disclosed polypeptides. The resulting antigen specific CD8+ CTL clones may be isolated from the patient, expanded using standard tissue culture techniques, and returned to the patient.

Alternatively, peptides corresponding to immunogenic portions of the polypeptides may be employed to generate tumor reactive T cell subsets by selective *in vitro* stimulation and expansion of autologous T cells to provide antigen-specific T cells which may be subsequently transferred to the patient as described, for example, by Chang *et al*, (*Crit. Rev. Oncol. Hematol.*, 22(3), 213, 1996). Cells of the immune system, such as T cells, may be isolated from the peripheral blood of a patient, using a commercially available cell separation system, such as CellPro Incorporated's (Bothell, WA) CEPRATE™ system (see U.S. Patent No. 5,240,856; U.S. Patent No. 5,215,926; WO 89/06280; WO 91/16116 and WO 92/07243). The separated cells are stimulated with one or more of the immunoreactive polypeptides contained within a delivery vehicle, such as a microsphere, to provide antigen-specific T cells. The population of tumor antigen-specific T cells is then expanded using

standard techniques and the cells are administered back to the patient.

In other embodiments, T-cell and/or antibody receptors specific for the polypeptides disclosed herein can be cloned, expanded, and transferred into other vectors or effector cells for use in adoptive immunotherapy. In particular, T cells may be transfected with the appropriate genes to express the variable domains from tumor specific monoclonal antibodies as the extracellular recognition elements and joined to the T cell receptor signaling chains, resulting in T cell activation, specific lysis, and cytokine release. This enables the T cell to redirect its specificity in an MHC-independent manner. See for example, Eshhar, Z., *Cancer Immunol Immunother*, 45(3-4):131-6, 1997 and Hwu, P., et al, *Cancer Res*, 55(15):3369-73, 1995. Another embodiment may include the transfection of tumor antigen specific alpha and beta T cell receptor chains into alternate T cells, as in Cole, DJ, et al, *Cancer Res*, 55(4):748-52, 1995.

In a further embodiment, syngeneic or autologous dendritic cells may be pulsed with peptides corresponding to at least an immunogenic portion of a polypeptide disclosed herein. The resulting antigen-specific dendritic cells may either be transferred into a patient, or employed to stimulate T cells to provide antigen-specific T cells which may, in turn, be administered to a patient. The use of peptide-pulsed dendritic cells to generate antigen-specific T cells and the subsequent use of such antigen-specific T cells to eradicate tumors in a murine model has been demonstrated by Cheever et al, *Immunological Reviews*, 157:177, 1997).

Furthermore, vectors expressing the disclosed polynucleotides may be introduced into stem cells taken from the patient and clonally propagated *in vitro* for autologous transplant back into the same patient.

Additionally, vectors expressing the disclosed polynucleotides may be introduced into stem cells taken from the patient and clonally propagated *in vitro* for autologous transplant back into the same patient. Polypeptides and fusion proteins of the present invention may also, or alternatively, be used to generate binding agents, such as antibodies or fragments thereof, that are capable of detecting metastatic human lung tumors. Binding agents of the present invention may generally be prepared using methods known to those of ordinary skill in the art, including the representative procedures described herein.

Binding agents are capable of differentiating between patients with and without lung cancer, using the representative assays described herein. In other words, antibodies or other binding agents raised against a lung tumor protein, or a suitable portion thereof, will generate a signal indicating the presence of primary or metastatic lung cancer in at least about 20% of patients afflicted with the disease, and will generate a negative signal indicating the absence of the disease in at least about 90% of individuals without primary or metastatic lung cancer. Suitable portions of such lung tumor proteins are portions that are able to generate a binding agent that indicates the presence of primary or metastatic lung cancer in substantially all (*i.e.*, at least about 80%, and preferably at least about 90%) of the patients for which lung cancer would be indicated using the full length protein, and that indicate the absence of lung cancer in substantially all of those samples that would be negative when tested with full length protein. The representative assays described below, such as the two-antibody sandwich assay, may generally be employed for evaluating the ability of a binding agent to detect metastatic human lung tumors.

The ability of a polypeptide prepared as described herein to generate antibodies capable of detecting primary or metastatic human lung tumors may generally be evaluated by raising one or more antibodies against the polypeptide (using, for example, a representative method described herein) and determining the ability of such antibodies to detect such tumors in patients. This determination may be made by assaying biological samples from patients with and without primary or metastatic lung cancer for the presence of a polypeptide that binds to the generated antibodies. Such test assays may be performed, for example, using a representative procedure described below. Polypeptides that generate antibodies capable of detecting at least 20% of primary or metastatic lung tumors by such procedures are considered to be useful in assays for detecting primary or metastatic human lung tumors. Polypeptide specific antibodies may be used alone or in combination to improve sensitivity.

Polypeptides capable of detecting primary or metastatic human lung tumors may be used as markers for diagnosing lung cancer or for monitoring disease progression in patients. In one embodiment, lung cancer in a patient may be diagnosed by evaluating a biological sample obtained from the patient for the level of one or more of the above

polypeptides, relative to a predetermined cut-off value. As used herein, suitable "biological samples" include blood, sera, urine and/or lung secretions.

The level of one or more of the above polypeptides may be evaluated using any binding agent specific for the polypeptide(s). A "binding agent," in the context of this invention, is any agent (such as a compound or a cell) that binds to a polypeptide as described above. As used herein, "binding" refers to a noncovalent association between two separate molecules (each of which may be free (*i.e.*, in solution) or present on the surface of a cell or a solid support), such that a "complex" is formed. Such a complex may be free or immobilized (either covalently or noncovalently) on a support material. The ability to bind may generally be evaluated by determining a binding constant for the formation of the complex. The binding constant is the value obtained when the concentration of the complex is divided by the product of the component concentrations. In general, two compounds are said to "bind" in the context of the present invention when the binding constant for complex formation exceeds about 10^3 L/mol. The binding constant may be determined using methods well known to those of ordinary skill in the art.

Any agent that satisfies the above requirements may be a binding agent. For example, a binding agent may be a ribosome with or without a peptide component, an RNA molecule or a peptide. In a preferred embodiment, the binding partner is an antibody, or a fragment thereof. Such antibodies may be polyclonal, or monoclonal. In addition, the antibodies may be single chain, chimeric, CDR-grafted or humanized. Antibodies may be prepared by the methods described herein and by other methods well known to those of skill in the art.

There are a variety of assay formats known to those of ordinary skill in the art for using a binding partner to detect polypeptide markers in a sample. *See, e.g.*, Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In a preferred embodiment, the assay involves the use of binding partner immobilized on a solid support to bind to and remove the polypeptide from the remainder of the sample. The bound polypeptide may then be detected using a second binding partner that contains a reporter group. Suitable second binding partners include antibodies that bind to the binding partner/polypeptide complex. Alternatively, a competitive assay may be utilized, in which a

polypeptide is labeled with a reporter group and allowed to bind to the immobilized binding partner after incubation of the binding partner with the sample. The extent to which components of the sample inhibit the binding of the labeled polypeptide to the binding partner is indicative of the reactivity of the sample with the immobilized binding partner.

The solid support may be any material known to those of ordinary skill in the art to which the antigen may be attached. For example, the solid support may be a test well in a microtiter plate or a nitrocellulose or other suitable membrane. Alternatively, the support may be a bead or disc, such as glass, fiberglass, latex or a plastic material such as polystyrene or polyvinylchloride. The support may also be a magnetic particle or a fiber optic sensor, such as those disclosed, for example, in U.S. Patent No. 5,359,681. The binding agent may be immobilized on the solid support using a variety of techniques known to those of skill in the art, which are amply described in the patent and scientific literature. In the context of the present invention, the term "immobilization" refers to both noncovalent association, such as adsorption, and covalent attachment (which may be a direct linkage between the antigen and functional groups on the support or may be a linkage by way of a cross-linking agent). Immobilization by adsorption to a well in a microtiter plate or to a membrane is preferred. In such cases, adsorption may be achieved by contacting the binding agent, in a suitable buffer, with the solid support for a suitable amount of time. The contact time varies with temperature, but is typically between about 1 hour and about 1 day. In general, contacting a well of a plastic microtiter plate (such as polystyrene or polyvinylchloride) with an amount of binding agent ranging from about 10 ng to about 10 μ g, and preferably about 100 ng to about 1 μ g, is sufficient to immobilize an adequate amount of binding agent.

Covalent attachment of binding agent to a solid support may generally be achieved by first reacting the support with a bifunctional reagent that will react with both the support and a functional group, such as a hydroxyl or amino group, on the binding agent. For example, the binding agent may be covalently attached to supports having an appropriate polymer coating using benzoquinone or by condensation of an aldehyde group on the support with an amine and an active hydrogen on the binding partner (*see, e.g.*, Pierce Immunotechnology Catalog and Handbook, 1991, at A12-A13).

In certain embodiments, the assay is a two-antibody sandwich assay. This assay may be performed by first contacting an antibody that has been immobilized on a solid support, commonly the well of a microtiter plate, with the sample, such that polypeptides within the sample are allowed to bind to the immobilized antibody. Unbound sample is then removed from the immobilized polypeptide-antibody complexes and a second antibody (containing a reporter group) capable of binding to a different site on the polypeptide is added. The amount of second antibody that remains bound to the solid support is then determined using a method appropriate for the specific reporter group.

More specifically, once the antibody is immobilized on the support as described above, the remaining protein binding sites on the support are typically blocked. Any suitable blocking agent known to those of ordinary skill in the art, such as bovine serum albumin or Tween 20™ (Sigma Chemical Co., St. Louis, MO). The immobilized antibody is then incubated with the sample, and polypeptide is allowed to bind to the antibody. The sample may be diluted with a suitable diluent, such as phosphate-buffered saline (PBS) prior to incubation. In general, an appropriate contact time (*i.e.*, incubation time) is that period of time that is sufficient to detect the presence of polypeptide within a sample obtained from an individual with lung cancer. Preferably, the contact time is sufficient to achieve a level of binding that is at least about 95% of that achieved at equilibrium between bound and unbound polypeptide. Those of ordinary skill in the art will recognize that the time necessary to achieve equilibrium may be readily determined by assaying the level of binding that occurs over a period of time. At room temperature, an incubation time of about 30 minutes is generally sufficient.

Unbound sample may then be removed by washing the solid support with an appropriate buffer, such as PBS containing 0.1% Tween 20™. The second antibody, which contains a reporter group, may then be added to the solid support. Preferred reporter groups include enzymes (such as horseradish peroxidase), substrates, cofactors, inhibitors, dyes, radionuclides, luminescent groups, fluorescent groups and biotin. The conjugation of antibody to reporter group may be achieved using standard methods known to those of ordinary skill in the art.

The second antibody is then incubated with the immobilized antibody-polypeptide complex for an amount of time sufficient to detect the bound polypeptide. An appropriate amount of time may generally be determined by assaying the level of binding that occurs over a period of time. Unbound second antibody is then removed and bound second antibody is detected using the reporter group. The method employed for detecting the reporter group depends upon the nature of the reporter group. For radioactive groups, scintillation counting or autoradiographic methods are generally appropriate. Spectroscopic methods may be used to detect dyes, luminescent groups and fluorescent groups. Biotin may be detected using avidin, coupled to a different reporter group (commonly a radioactive or fluorescent group or an enzyme). Enzyme reporter groups may generally be detected by the addition of substrate (generally for a specific period of time), followed by spectroscopic or other analysis of the reaction products.

To determine the presence or absence of lung cancer, the signal detected from the reporter group that remains bound to the solid support is generally compared to a signal that corresponds to a predetermined cut-off value. In one preferred embodiment, the cut-off value is the average mean signal obtained when the immobilized antibody is incubated with samples from patients without lung cancer. In general, a sample generating a signal that is three standard deviations above the predetermined cut-off value is considered positive for lung cancer. In an alternate preferred embodiment, the cut-off value is determined using a Receiver Operator Curve, according to the method of Sackett et al., *Clinical Epidemiology: A Basic Science for Clinical Medicine*, Little Brown and Co., 1985, p. 106-7. Briefly, in this embodiment, the cut-off value may be determined from a plot of pairs of true positive rates (*i.e.*, sensitivity) and false positive rates (100%-specificity) that correspond to each possible cut-off value for the diagnostic test result. The cut-off value on the plot that is the closest to the upper left-hand corner (*i.e.*, the value that encloses the largest area) is the most accurate cut-off value, and a sample generating a signal that is higher than the cut-off value determined by this method may be considered positive. Alternatively, the cut-off value may be shifted to the left along the plot, to minimize the false positive rate, or to the right, to minimize the false negative rate. In general, a sample generating a signal that is higher than the cut-off value determined by this method is considered positive for lung cancer.

In a related embodiment, the assay is performed in a flow-through or strip test format, wherein the antibody is immobilized on a membrane, such as nitrocellulose. In the flow-through test, polypeptides within the sample bind to the immobilized antibody as the sample passes through the membrane. A second, labeled antibody then binds to the antibody-polypeptide complex as a solution containing the second antibody flows through the membrane. The detection of bound second antibody may then be performed as described above. In the strip test format, one end of the membrane to which antibody is bound is immersed in a solution containing the sample. The sample migrates along the membrane through a region containing second antibody and to the area of immobilized antibody. Concentration of second antibody at the area of immobilized antibody indicates the presence of lung cancer. Typically, the concentration of second antibody at that site generates a pattern, such as a line, that can be read visually. The absence of such a pattern indicates a negative result. In general, the amount of antibody immobilized on the membrane is selected to generate a visually discernible pattern when the biological sample contains a level of polypeptide that would be sufficient to generate a positive signal in the two-antibody sandwich assay, in the format discussed above. Preferably, the amount of antibody immobilized on the membrane ranges from about 25 ng to about 1 μ g, and more preferably from about 50 ng to about 500 ng. Such tests can typically be performed with a very small amount of biological sample.

Of course, numerous other assay protocols exist that are suitable for use with the antigens or antibodies of the present invention. The above descriptions are intended to be exemplary only.

In another embodiment, the above polypeptides may be used as markers for the progression of lung cancer. In this embodiment, assays as described above for the diagnosis of lung cancer may be performed over time, and the change in the level of reactive polypeptide(s) evaluated. For example, the assays may be performed every 24-72 hours for a period of 6 months to 1 year, and thereafter performed as needed. In general, lung cancer is progressing in those patients in whom the level of polypeptide detected by the binding agent increases over time. In contrast, lung cancer is not progressing when the level of reactive polypeptide either remains constant or decreases with time.

Antibodies for use in the above methods may be prepared by any of a variety of techniques known to those of ordinary skill in the art. See, e.g., Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In one such technique, an immunogen comprising the antigenic polypeptide is initially injected into any of a wide variety of mammals (e.g., mice, rats, rabbits, sheep and goats). In this step, the polypeptides of this invention may serve as the immunogen without modification. Alternatively, particularly for relatively short polypeptides, a superior immune response may be elicited if the polypeptide is joined to a carrier protein, such as bovine serum albumin or keyhole limpet hemocyanin. The immunogen is injected into the animal host, preferably according to a predetermined schedule incorporating one or more booster immunizations, and the animals are bled periodically. Polyclonal antibodies specific for the polypeptide may then be purified from such antisera by, for example, affinity chromatography using the polypeptide coupled to a suitable solid support.

Monoclonal antibodies specific for the antigenic polypeptide of interest may be prepared, for example, using the technique of Kohler and Milstein, *Eur. J. Immunol.* 6:511-519, 1976, and improvements thereto. Briefly, these methods involve the preparation of immortal cell lines capable of producing antibodies having the desired specificity (i.e., reactivity with the polypeptide of interest). Such cell lines may be produced, for example, from spleen cells obtained from an animal immunized as described above. The spleen cells are then immortalized by, for example, fusion with a myeloma cell fusion partner, preferably one that is syngeneic with the immunized animal. A variety of fusion techniques may be employed. For example, the spleen cells and myeloma cells may be combined with a nonionic detergent for a few minutes and then plated at low density on a selective medium that supports the growth of hybrid cells, but not myeloma cells. A preferred selection technique uses HAT (hypoxanthine, aminopterin, thymidine) selection. After a sufficient time, usually about 1 to 2 weeks, colonies of hybrids are observed. Single colonies are selected and tested for binding activity against the polypeptide. Hybridomas having high reactivity and specificity are preferred.

Monoclonal antibodies may be isolated from the supernatants of growing hybridoma colonies. In addition, various techniques may be employed to enhance the yield,

such as injection of the hybridoma cell line into the peritoneal cavity of a suitable vertebrate host, such as a mouse. Monoclonal antibodies may then be harvested from the ascites fluid or the blood. Contaminants may be removed from the antibodies by conventional techniques, such as chromatography, gel filtration, precipitation, and extraction. The polypeptides of this invention may be used in the purification process in, for example, an affinity chromatography step.

Monoclonal antibodies of the present invention may also be used as therapeutic reagents, to diminish or eliminate lung tumors. The antibodies may be used on their own (for instance, to inhibit metastases) or coupled to one or more therapeutic agents. Suitable agents in this regard include radionuclides, differentiation inducers, drugs, toxins, and derivatives thereof. Preferred radionuclides include ^{90}Y , ^{123}I , ^{125}I , ^{131}I , ^{186}Re , ^{188}Re , ^{211}At , and ^{212}Bi . Preferred drugs include methotrexate, and pyrimidine and purine analogs. Preferred differentiation inducers include phorbol esters and butyric acid. Preferred toxins include ricin, abrin, diphtheria toxin, cholera toxin, gelonin, *Pseudomonas* exotoxin, *Shigella* toxin, and pokeweed antiviral protein.

A therapeutic agent may be coupled (*e.g.*, covalently bonded) to a suitable monoclonal antibody either directly or indirectly (*e.g.*, via a linker group). A direct reaction between an agent and an antibody is possible when each possesses a substituent capable of reacting with the other. For example, a nucleophilic group, such as an amino or sulfhydryl group, on one may be capable of reacting with a carbonyl-containing group, such as an anhydride or an acid halide, or with an alkyl group containing a good leaving group (*e.g.*, a halide) on the other.

Alternatively, it may be desirable to couple a therapeutic agent and an antibody via a linker group. A linker group can function as a spacer to distance an antibody from an agent in order to avoid interference with binding capabilities. A linker group can also serve to increase the chemical reactivity of a substituent on an agent or an antibody, and thus increase the coupling efficiency. An increase in chemical reactivity may also facilitate the use of agents, or functional groups on agents, which otherwise would not be possible.

It will be evident to those skilled in the art that a variety of bifunctional or polyfunctional reagents, both homo- and hetero-functional (such as those described in the

catalog of the Pierce Chemical Co., Rockford, IL), may be employed as the linker group. Coupling may be effected, for example, through amino groups, carboxyl groups, sulfhydryl groups or oxidized carbohydrate residues. There are numerous references describing such methodology, *e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.

Where a therapeutic agent is more potent when free from the antibody portion of the immunoconjugates of the present invention, it may be desirable to use a linker group which is cleavable during or upon internalization into a cell. A number of different cleavable linker groups have been described. The mechanisms for the intracellular release of an agent from these linker groups include cleavage by reduction of a disulfide bond (*e.g.*, U.S. Patent No. 4,489,710, to Spitler), by irradiation of a photolabile bond (*e.g.*, U.S. Patent No. 4,625,014, to Senter et al.), by hydrolysis of derivatized amino acid side chains (*e.g.*, U.S. Patent No. 4,638,045, to Kohn et al.), by serum complement-mediated hydrolysis (*e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.), and acid-catalyzed hydrolysis (*e.g.*, U.S. Patent No. 4,569,789, to Blattler et al.).

It may be desirable to couple more than one agent to an antibody. In one embodiment, multiple molecules of an agent are coupled to one antibody molecule. In another embodiment, more than one type of agent may be coupled to one antibody. Regardless of the particular embodiment, immunoconjugates with more than one agent may be prepared in a variety of ways. For example, more than one agent may be coupled directly to an antibody molecule, or linkers which provide multiple sites for attachment can be used. Alternatively, a carrier can be used.

A carrier may bear the agents in a variety of ways, including covalent bonding either directly or via a linker group. Suitable carriers include proteins such as albumins (*e.g.*, U.S. Patent No. 4,507,234, to Kato et al.), peptides and polysaccharides such as aminodextran (*e.g.*, U.S. Patent No. 4,699,784, to Shih et al.). A carrier may also bear an agent by noncovalent bonding or by encapsulation, such as within a liposome vesicle (*e.g.*, U.S. Patent Nos. 4,429,008 and 4,873,088). Carriers specific for radionuclide agents include radiohalogenated small molecules and chelating compounds. For example, U.S. Patent No. 4,735,792 discloses representative radiohalogenated small molecules and their synthesis. A radionuclide chelate may be formed from chelating compounds that include those containing

nitrogen and sulfur atoms as the donor atoms for binding the metal, or metal oxide, radionuclide. For example, U.S. Patent No. 4,673,562, to Davison et al. discloses representative chelating compounds and their synthesis.

A variety of routes of administration for the antibodies and immunoconjugates may be used. Typically, administration will be intravenous, intramuscular, subcutaneous or in the bed of a resected tumor. It will be evident that the precise dose of the antibody/immunoconjugate will vary depending upon the antibody used, the antigen density on the tumor, and the rate of clearance of the antibody.

Diagnostic reagents of the present invention may also comprise polynucleotide sequences encoding one or more of the above polypeptides, or one or more portions thereof. For example, at least two oligonucleotide primers may be employed in a polymerase chain reaction (PCR) based assay to amplify lung tumor-specific cDNA derived from a biological sample, wherein at least one of the oligonucleotide primers is specific for a polynucleotide molecule encoding a lung tumor protein of the present invention. The presence of the amplified cDNA is then detected using techniques well known in the art, such as gel electrophoresis. Similarly, oligonucleotide probes specific for a polynucleotide molecule encoding a lung tumor protein of the present invention may be used in a hybridization assay to detect the presence of an inventive polypeptide in a biological sample.

As used herein, the term "oligonucleotide primer/probe specific for a polynucleotide molecule" means an oligonucleotide sequence that has at least about 60%, preferably at least about 75% and more preferably at least about 90%, identity to the polynucleotide molecule in question. Oligonucleotide primers and/or probes which may be usefully employed in the inventive diagnostic methods preferably have at least about 10-40 nucleotides. In a preferred embodiment, the oligonucleotide primers comprise at least about 10 contiguous nucleotides of a polynucleotide molecule comprising sequence selected from SEQ ID NO: 1-109, 111, 113 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168 and 171. Preferably, oligonucleotide probes for use in the inventive diagnostic methods comprise at least about 15 contiguous oligonucleotides of a polynucleotide molecule comprising a sequence provided in SEQ ID NO: 1-109, 111, 113 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168 and 171. Techniques for both PCR based assays and hybridization assays are

well known in the art (see, for example, Mullis *et al. Ibid*; Ehrlich, *Ibid*). Primers or probes may thus be used to detect lung tumor-specific sequences in biological samples, including blood, semen, lung tissue and/or lung tumor tissue.

The following Examples are offered by way of illustration and not by way of limitation.

EXAMPLES

Example 1

ISOLATION AND CHARACTERIZATION OF cDNA SEQUENCES ENCODING LUNG TUMOR POLYPEPTIDES

This example illustrates the isolation of cDNA molecules encoding lung tumor-specific polypeptides from lung tumor cDNA libraries.

A. Isolation of cDNA Sequences from a Lung Squamous Cell Carcinoma Library

A human lung squamous cell carcinoma cDNA expression library was constructed from poly A⁺ RNA from a pool of two patient tissues using a Superscript Plasmid System for cDNA Synthesis and Plasmid Cloning kit (BRL Life Technologies, Gaithersburg, MD) following the manufacturer's protocol. Specifically, lung carcinoma tissues were homogenized with polytron (Kinematica, Switzerland) and total RNA was extracted using Trizol reagent (BRL Life Technologies) as directed by the manufacturer. The poly A⁺ RNA was then purified using an oligo dT cellulose column as described in Sambrook *et al.*, *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989. First-strand cDNA was synthesized using the NotI/Oligo-dT18 primer. Double-stranded cDNA was synthesized, ligated with BstXI/EcoRI adaptors (Invitrogen, San Diego, CA) and digested with NotI. Following size fractionation with cDNA size fractionation columns (BRL Life Technologies), the cDNA was ligated into the BstXI/NotI

site of pcDNA3.1 (Invitrogen) and transformed into ElectroMax *E. coli* DH10B cells (BRL Life Technologies) by electroporation.

Using the same procedure, a normal human lung cDNA expression library was prepared from a pool of four tissue specimens. The cDNA libraries were characterized by determining the number of independent colonies, the percentage of clones that carried insert, the average insert size and by sequence analysis. The lung squamous cell carcinoma library contained 2.7×10^6 independent colonies, with 100% of clones having an insert and the average insert size being 2100 base pairs. The normal lung cDNA library contained 1.4×10^6 independent colonies, with 90% of clones having inserts and the average insert size being 1800 base pairs. For both libraries, sequence analysis showed that the majority of clones had a full length cDNA sequence and were synthesized from mRNA.

cDNA library subtraction was performed using the above lung squamous cell carcinoma and normal lung cDNA libraries, as described by Hara *et al.* (*Blood*, 84:189-199, 1994) with some modifications. Specifically, a lung squamous cell carcinoma-specific subtracted cDNA library was generated as follows. Normal tissue cDNA library (80 μ g) was digested with BamHI and XhoI, followed by a filling-in reaction with DNA polymerase Klenow fragment. After phenol-chloroform extraction and ethanol precipitation, the DNA was dissolved in 133 μ l of H₂O, heat-denatured and mixed with 133 μ l (133 μ g) of Photoprobe biotin (Vector Laboratories, Burlingame, CA). As recommended by the manufacturer, the resulting mixture was irradiated with a 270 W sunlamp on ice for 20 minutes. Additional Photoprobe biotin (67 μ l) was added and the biotinylation reaction was repeated. After extraction with butanol five times, the DNA was ethanol-precipitated and dissolved in 23 μ l H₂O to form the driver DNA.

To form the tracer DNA, 10 μ g lung squamous cell carcinoma cDNA library was digested with NotI and SpeI, phenol chloroform extracted and passed through Chroma spin-400 columns (Clontech, Palo Alto, CA). Typically, 5 μ g of cDNA was recovered after the sizing column. Following ethanol precipitation, the tracer DNA was dissolved in 5 μ l H₂O. Tracer DNA was mixed with 15 μ l driver DNA and 20 μ l of 2 x hybridization buffer (1.5 M NaCl/10 mM EDTA/50 mM HEPES pH 7.5/0.2% sodium dodecyl sulfate), overlaid with mineral oil, and heat-denatured completely. The sample was immediately transferred

into a 68 °C water bath and incubated for 20 hours (long hybridization [LH]). The reaction mixture was then subjected to a streptavidin treatment followed by phenol/chloroform extraction. This process was repeated three more times. Subtracted DNA was precipitated, dissolved in 12 µl H₂O, mixed with 8 µl driver DNA and 20 µl of 2 x hybridization buffer, and subjected to a hybridization at 68 °C for 2 hours (short hybridization [SH]). After removal of biotinylated double-stranded DNA, subtracted cDNA was ligated into NotI/SpeI site of chloramphenicol resistant pBCSK⁺ (Stratagene, La Jolla, CA) and transformed into ElectroMax *E. coli* DH10B cells by electroporation to generate a lung squamous cell carcinoma specific subtracted cDNA library (herein after referred to as "lung subtraction I").

A second lung squamous cell carcinoma specific subtracted cDNA library (referred to as "lung subtraction II") was generated in a similar way to the lung subtraction library I, except that eight frequently recovered genes from lung subtraction I were included in the driver DNA, and 24,000 independent clones were recovered.

To analyze the subtracted cDNA libraries, plasmid DNA was prepared from 320 independent clones, randomly picked from the subtracted lung squamous cell carcinoma specific libraries. Representative cDNA clones were further characterized by DNA sequencing with a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A and/or Model 377 (Foster City, CA). The cDNA sequences for sixty isolated clones are provided in SEQ ID NO: 1-60. These sequences were compared to known sequences in the gene bank using the EMBL and GenBank databases (release 96). No significant homologies were found to the sequences provided in SEQ ID NO: 2, 3, 19, 38 and 46. The sequences of SEQ ID NO: 1, 6-8, 10-13, 15, 17, 18, 20-27, 29, 30, 32, 34-37, 39-45, 47-49, 51, 52, 54, 55 and 57-59 were found to show some homology to previously identified expressed sequence tags (ESTs). The sequences of SEQ ID NO: 9, 28, 31 and 33 were found to show some homology to previously identified non-human gene sequences and the sequences of SEQ ID NO: 4, 5, 14, 50, 53, 56 and 60 were found to show some homology to gene sequences previously identified in humans.

The subtraction procedure described above was repeated using the above lung squamous cell carcinoma cDNA library as the tracer DNA, and the above normal lung tissue cDNA library and a cDNA library from normal liver and heart (constructed from a pool of

one sample of each tissue as described above), plus twenty other cDNA clones that were frequently recovered in lung subtractions I and II, as the driver DNA (lung subtraction III). The normal liver and heart cDNA library contained 1.76×10^6 independent colonies, with 100% of clones having inserts and the average insert size being 1600 base pairs. Ten additional clones were isolated (SEQ ID NO: 61-70). Comparison of these cDNA sequences with those in the gene bank as described above, revealed no significant homologies to the sequences provided in SEQ ID NO: 62 and 67. The sequences of SEQ ID NO: 61, 63-66, 68 and 69 were found to show some homology to previously isolated ESTs and the sequence provided in SEQ ID NO: 70 was found to show some homology to a previously identified rat gene.

B. Isolation of cDNA Sequences from a Lung Adenocarcinoma Library

A human lung adenocarcinoma cDNA expression library was constructed as described above. The library contained 3.2×10^6 independent colonies, with 100% of clones having an insert and the average insert size being 1500 base pairs. Library subtraction was performed as described above using the normal lung and normal liver and heart cDNA expression libraries described above as the driver DNA. Twenty-six hundred independent clones were recovered.

Initial cDNA sequence analysis from 100 independent clones revealed many ribosomal protein genes. The cDNA sequences for fifteen clones isolated in this subtraction are provided in SEQ ID NO: 71-86. Comparison of these sequences with those in the gene bank as described above revealed no significant homologies to the sequence provided in SEQ ID NO: 84. The sequences of SEQ ID NO: 71, 73, 74, 77, 78 and 80-82 were found to show some homology to previously isolated ESTs, and the sequences of SEQ ID NO: 72, 75, 76, 79, 83 and 85 were found to show some homology to previously identified human genes.

Example 2

DETERMINATION OF TISSUE SPECIFICITY OF LUNG TUMOR POLYPEPTIDES

Using gene specific primers, mRNA expression levels for seven representative lung tumor polypeptides described in Example 1 were examined in a variety of normal and tumor tissues using RT-PCR.

Briefly, total RNA was extracted from a variety of normal and tumor tissues using Trizol reagent as described above. First strand synthesis was carried out using 2 µg of total RNA with SuperScript II reverse transcriptase (BRL Life Technologies) at 42 °C for one hour. The cDNA was then amplified by PCR with gene-specific primers. To ensure the semi-quantitative nature of the RT-PCR, β-actin was used as an internal control for each of the tissues examined. 1 µl of 1:30 dilution of cDNA was employed to enable the linear range amplification of the β-actin template and was sensitive enough to reflect the differences in the initial copy numbers. Using these conditions, the β-actin levels were determined for each reverse transcription reaction from each tissue. DNA contamination was minimized by DNase treatment and by assuring a negative PCR result when using first strand cDNA that was prepared without adding reverse transcriptase.

mRNA Expression levels were examined in five different types of tumor tissue (lung squamous cell carcinoma from 3 patients, lung adenocarcinoma, colon tumor from 2 patients, breast tumor and prostate tumor), and thirteen different normal tissues (lung from 4 donors, prostate, brain, kidney, liver, ovary, skeletal muscle, skin, small intestine, stomach, myocardium, retina and testes). Using a 10-fold amount of cDNA, the antigen LST-S1-90 (SEQ ID NO: 3) was found to be expressed at high levels in lung squamous cell carcinoma and in breast tumor, and at low to undetectable levels in the other tissues examined.

The antigen LST-S2-68 (SEQ ID NO: 15) appears to be specific to lung and breast tumor, however, expression was also detected in normal kidney. Antigens LST-S1-169 (SEQ ID NO: 6) and LST-S1-133 (SEQ ID NO: 5) appear to be very abundant in lung tissues (both normal and tumor), with the expression of these two genes being decreased in most of the normal tissues tested. Both LST-S1-169 and LST-S1-133 were also expressed in breast and colon tumors. Antigens LST-S1-6 (SEQ ID NO: 7) and LST-S2-I2-5F (SEQ ID NO: 47) did not show tumor or tissue specific expression, with the expression of LST-S1-28 being rare and only detectable in a few tissues. The antigen LST-S3-7 (SEQ ID NO: 63) showed lung and breast tumor specific expression, with its message only being detected in

normal testes when the PCR was performed for 30 cycles. Lower level expression was detected in some normal tissues when the cycle number was increased to 35. Antigen LST-S3-13 (SEQ ID NO: 66) was found to be expressed in 3 out of 4 lung tumors, one breast tumor and both colon tumor samples. Its expression in normal tissues was lower compared to tumors, and was only detected in 1 out of 4 normal lung tissues and in normal tissues from kidney, ovary and retina. Expression of antigens LST-S3-4 (SEQ ID NO: 62) and LST-S3-14 (SEQ ID NO: 67) was rare and did not show any tissue or tumor specificity. Consistent with Northern blot analyses, the RT-PCT results on antigen LAT-S1-A-10A (SEQ ID NO: 78) suggested that its expression is high in lung, colon, stomach and small intestine tissues, including lung and colon tumors, whereas its expression was low or undetectable in other tissues.

A total of 2002 cDNA fragments isolated in lung subtractions I, II and III, described above, were colony PCR amplified and their mRNA expression levels in lung tumor, normal lung, and various other normal and tumor tissues were determined using microarray technology (Synteni, Palo Alto, CA). Briefly, the PCR amplification products were dotted onto slides in an array format, with each product occupying a unique location in the array. mRNA was extracted from the tissue sample to be tested, reverse transcribed, and fluorescent-labeled cDNA probes were generated. The microarrays were probed with the labeled cDNA probes, the slides scanned and fluorescence intensity was measured. This intensity correlates with the hybridization intensity. Seventeen non-redundant cDNA clones showed over-expression in lung squamous tumors, with expression in normal tissues tested (lung, skin, lymph node, colon, liver, pancreas, breast, heart, bone marrow, large intestine, kidney, stomach, brain, small intestine, bladder and salivary gland) being either undetectable, or 10-fold less compared to lung squamous tumors. The determined partial cDNA sequences for the clone L513S are provided in SEQ ID NO: 87 and 88; those for L514S are provided in SEQ ID NO: 89 and 90; those for L516S in SEQ ID NO: 91 and 92; that for L517S in SEQ ID NO: 93; that for L519S in SEQ ID NO: 94; those for L520S in SEQ ID NO: 95 and 96; those for L521S in SEQ ID NO: 97 and 98; that for L522S in SEQ ID NO: 99; that for L523S in SEQ ID NO: 100; that for L524S in SEQ ID NO: 101; that for L525S in SEQ ID NO: 102; that for L526S in SEQ ID NO: 103; that for L527S in SEQ ID NO: 104; that for L528S in

SEQ ID NO: 105; that for L529S in SEQ ID NO: 106; and those for L530S in SEQ ID NO: 107 and 108. Additionally, the full-length cDNA sequences for L503S and L514S (variants 1 and 2), are provided in SEQ ID NO: 151, 153 and 154, respectively, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 152, 155 and 156. Due to polymorphisms, the clone L531S appears to have two forms. A first determined full-length cDNA sequence for L531S is provided in SEQ ID NO: 109, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 110. A second determined full-length cDNA sequence for L531S is provided in SEQ ID NO: 111, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 112. The sequence of SEQ ID NO: 111 is identical to that of SEQ ID NO: 109, except that it contains a 27 bp insertion. Similarly, L514S also has two alternatively spliced forms; the first variant cDNA is listed as SEQ ID NO: 153, with the corresponding amino acid sequence as SEQ ID NO: 155. The second variant form of L514S full-length cDNA is referred to as SEQ ID NO: 154, with its corresponding amino acid sequence as SEQ ID NO: 156.

Full length cloning for L524S (SEQ ID NO: 101) yielded two variants (SEQ ID NO: 163 and 164) with the corresponding predicted amino acid sequences (SEQ ID NO: 165 and 166), respectively. Both variants have been shown to encode parathyroid hormone-related peptide.

Comparison of the sequences of L514S and L531S (SEQ ID NO: 87 and 88, 89 and 90, and 109, respectively) with those in the gene bank, as described above, revealed no significant homologies to known sequences. The sequences of L513S, L516S, L517S, L519S, L520S and L530S (SEQ ID NO: 87 and 88, 91 and 92, 93, 94, 95 and 96, 107 and 108, respectively) were found to show some homology to previously identified ESTs. The sequences of L521S, L522S, L523S, L524S, L525S, L526S, L527S, L528S and L529S (SEQ ID NO: 97 and 98, 99, 99, 101, 102, 103, 104, 105, and 106, respectively) were found to represent known genes. The determined full-length cDNA sequences for L520S is provided in SEQ ID NO: 113, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 114. Subsequent microarray analysis has shown L520S to be overexpressed in breast tumors in addition to lung squamous tumors.

Further analysis has demonstrated L529S (SEQ ID NO: 106 and 115), L525S (SEQ ID NO: 102 and 120) and L527S (SEQ ID NO: 104) are cytoskeletal components and potentially squamous cell specific proteins. L529S is connexin 26, a gap junction protein. It is highly expressed in lung squamous tumor 9688T, and moderately over-expressed in two others. However, lower level expression of connexin 26 is also detectable in normal skin, colon, liver and stomach. The over-expression of connexin 26 in some breast tumors has been reported and a mutated form of L529S may result in over-expression in lung tumors. L525S is plakophilin 1, a desmosomal protein found in plaque-bearing adhering junctions of the skin. Expression levels for L525S mRNA is highly elevated in three out of four lung squamous tumors tested, and in normal skin. L527S has been identified as keratin 6 isoform, type II 58 Kd keratin, and cytokeratin 13 and shows over-expression in squamous tumors and low expression in normal skin, breast and colon tissues. Notably, keratin and keratin-related genes have been extensively documented as potential markers for lung cancer including CYFRA2.1 (Pastor, A., et al, *Eur. Respir. J.*, 10:603-609, 1997). L513S (SEQ ID NO: 87 and 88) shows moderate over-expression in several tumor tissues tested, and encodes a protein that was first isolated as a pemphigus vulgaris antigen.

L520S (SEQ ID NO: 95 and 96) and L521S (SEQ ID NO: 97 and 98) are highly expressed in lung squamous tumors, and L520S is up-regulated in normal salivary gland and L521S is over-expressed in normal skin. Both belong to a family of small proline rich proteins and represent markers for fully differentiated squamous cells. L521S has been described as a specific marker for lung squamous tumor (Hu, R., et al, *Lung Cancer*, 20:25-30, 1998). L515S (SEQ ID NO: 162) encodes IGF- β 2 and L516S is an aldose reductase homologue and both are moderately expressed in lung squamous tumors and in normal colon. Notably, L516S (SEQ ID NO: 91 and 92) is up-regulated in metastatic tumors but not primary lung adenocarcinoma, an indication of its potential role in metastasis and a potential prognostic marker. L522S (SEQ ID NO: 99) is moderately over-expressed in lung squamous tumors with minimum expression in normal tissues. L522S has been shown to belong to a class IV alcohol dehydrogenase, ADH7, and its expression profile suggests it is a squamous cell specific antigen. L523S (SEQ ID NO: 100) is moderately over-expressed in lung

squamous tumor, human pancreatic cancer cell lines and pancreatic cancer tissues, suggesting this gene may be a shared antigen between pancreatic and lung squamous cell cancer.

L524S (SEQ ID NO: 101) is over-expressed in the majority of squamous tumors tested and is homologous with parathyroid hormone-related peptide (PTHrP), which is best known to cause humoral hypercalcaemia associated with malignant tumors such as leukemia, prostate and breast cancer. It is also believed that PTHrP is most commonly associated with squamous carcinoma of lung and rarely with lung adenocarcinoma (Davidson, L.A., et al, *J. Pathol.*, 178: 398-401, 1996). L528S (SEQ ID NO: 105) is highly over-expressed in two lung squamous tumors with moderate expression in two other squamous tumors, one lung adenocarcinoma and some normal tissues, including skin, lymph nodes, heart, stomach and lung. It encodes the NMB gene that is similar to the precursor of melanocyte specific gene Pmel17, which is reported to be preferentially expressed in low-metastatic potential melanoma cell lines. This suggests that L528S may be a shared antigen in both melanoma and lung squamous cell carcinoma. L526S (SEQ ID NO: 103) is overexpressed in all lung squamous cell tumor tissues tested and has been shown to share homology with a gene (ATM) in which a mutation causes ataxia telangiectasia, a genetic disorder in humans causing a predisposition to cancer, among other symptoms. ATM encodes a protein that activates p53 mediated cell-cycle checkpoint through direct binding and phosphorylation of the p53 molecule. Approximately 40% of lung cancer is associated with p53 mutations, and it is speculated that over-expression of ATM is a result of compensation for loss of p53 function, but it is unknown whether over-expression is the cause or result of lung squamous cell carcinoma. Additionally, expression of L526S (ATM) is also detected in a metastatic but not lung adenocarcinoma, suggesting a role in metastasis.

Example 3

ISOLATION AND CHARACTERIZATION OF LUNG TUMOR POLYPEPTIDES BY PCR-BASED SUBTRACTION

Eight hundred and fifty seven clones from a cDNA subtraction library, containing cDNA from a pool of two human lung squamous tumors subtracted against eight

normal human tissue cDNAs including lung, PBMC, brain, heart, kidney, liver, pancreas, and skin, (Clontech, Palo Alto, CA) were derived and submitted to a first round of PCR amplification. This library was subjected to a second round of PCR amplification, following the manufacturer's protocol. The resulting cDNA fragments were subcloned into the vector P7- Adv vector (Clontech, Palo Alto, CA) and transformed into DH5 α *E. coli* (Gibco, BRL). DNA was isolated from independent clones and sequenced using a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A.

One hundred and sixty two positive clones were sequenced. Comparison of the DNA sequences of these clones with those in the gene bank using the EMBL and GenBank databases, as described above, revealed no significant homologies to 13 of these clones, hereinafter referred to as Contig 13, 16, 17, 19, 22, 24, 29, 47, 49, 56-59. The determined cDNA sequences for these clones are provided in SEQ ID NO: 125, 127-129, 131-133, 142, 144, 148-150, and 157, respectively. Contigs 1, 3-5, 7-10, 12, 11, 15, 20, 31, 33, 38, 39, 41, 43, 44, 45, 48, 50, 53, 54 (SEQ ID NO: 115-124, 126, 130, 134-141, 143, 145-147, respectively) were found to show some degree of homology to previously identified DNA sequences. Contig 57 (SEQ ID NO: 149) was found to represent the clone L519S (SEQ ID NO: 94) disclosed in US. Patent Application No. 09/123,912, filed July 27, 1998. To the best of the inventors' knowledge, none of these sequences have been previously shown to be differentially over-expressed in lung tumors.

mRNA expression levels for representative clones in lung tumor tissues, normal lung tissues (n=4), resting PBMC, salivary gland, heart, stomach, lymph nodes, skeletal muscle, soft palate, small intestine, large intestine, bronchial, bladder, tonsil, kidney, esophagus, bone marrow, colon, adrenal gland, pancreas, and skin, (all derived from human) were determined by RT-PCR as described above. Expression levels using microarray technology, as described above, were examined in one sample of each tissue type unless otherwise indicated.

Contig 3 (SEQ ID NO: 116) was found to be highly expressed in all head and neck squamous cell tumors tested (17/17), and expressed in the majority (8/12) of lung squamous tumors, (high expression in 7/12, moderate in 2/12, and low in 2/12), while showing negative expression for 2/4 normal lung tissues and low expression in the remaining

two samples. Contig 3 showed moderate expression in skin and soft palate, and lowered expression levels in resting PBMC, large intestine, salivary gland, tonsil, pancreas, esophagus, and colon. Contig 11 (SEQ ID NO: 124) was found to be expressed in all head and neck squamous cell tumors tested (17/17): highly expressed in 14/17, and moderately expressed in 3/17. Additionally, expression in lung squamous tumors showed high expression in 3/12 and moderate in 4/12. Contig 11 was negative for 3/4 normal lung samples, with the remaining sample having only low expression. Contig 11 showed low to moderate reactivity to salivary gland, soft palate, bladder, tonsil, skin, esophagus, and large intestine. Contig 13 (SEQ ID NO: 125) was found to be expressed in all head and neck squamous cell tumors tested (17/17): highly expressed in 12/17, and moderately expressed in 5/17. Contig 13 was expressed in 7/12 lung squamous tumors, with high expression in 4/12 and moderate expression in three samples. Analysis of normal lung samples showed negative expression for 2/4 and low to moderate expression in the remaining two samples. Contig 13 did show low to moderate reactivity to resting PBMC, salivary gland, bladder, pancreas, tonsil, skin, esophagus, and large intestine, as well as high expression in soft palate. Contig 16 (SEQ ID NO: 127) was found to be moderately expressed in some head and neck squamous cell tumors (6/17) and one lung squamous tumor; while showing no expression in any normal lung samples tested. Contig 16 did show low reactivity to resting PBMC, large intestine, skin, salivary gland, and soft palate. Contig 17 (SEQ ID NO: 128) was shown to be expressed in all head and neck squamous cell tumors tested (17/17): highly expressed in 5/17, and moderately expressed in 12/17. Expression levels in lung squamous tumors showed one tumor sample with high expression and 3/12 with moderate levels. Contig 17 was negative for 2/4 normal lung samples, with the remaining samples having only low expression. Additionally, low level expression was found in esophagus and soft palate. Contig 19 (SEQ ID NO: 129) was found to be expressed in most head and neck squamous cell tumors tested (11/17): with two samples having high levels, 6/17 showing moderate expression, and low expression being found in 3/17. Testing in lung squamous tumors revealed only moderate expression in 3/12 samples. Expression levels in 2/4 of normal lung samples were negative, the two other samples having only low expression. Contig 19 did show low expression levels in esophagus, resting PBMC, salivary gland, bladder, soft palate, and pancreas.

Contig 22, (SEQ ID NO: 131) was shown to be expressed in most head and neck squamous cell tumors tested (13/17) with high expression in four of these samples, moderate expression in 6/17, and low expression in 3/17. Expression levels in lung squamous tumors were found to be moderate to high for 3/12 tissues tested, with negative expression in two normal lung samples and low expression in two other samples (n=4). Contig 22 did show low expression in skin, salivary gland and soft palate. Similarly, Contig 24 (SEQ ID NO: 132) was found to be expressed in most head and neck squamous cell tumors tested (13/17) with high expression in three of these samples, moderate expression in 6/17, and low expression in 4/17. Expression levels in lung squamous tumors were found to be moderate to high for 3/12 tissues tested, with negative expression for three normal lung samples and low expression in one sample (n=4). Contig 24 did show low expression in skin, salivary gland and soft palate. Contig 29 (SEQ ID NO: 133) was expressed in nearly all head and neck squamous cell tumors tested (16/17): highly expressed in 4/17, moderately expressed in 11/17, with low expression in one sample. Also, it was moderately expressed in 3/12 lung squamous tumors, while being negative for 2/4 normal lung samples. Contig 29 showed low to moderate expression in large intestine, skin, salivary gland, pancreas, tonsil, heart and soft palate. Contig 47 (SEQ ID NO: 142) was expressed in most head and neck squamous cell tumors tested (12/17): moderate expression in 10/17, and low expression in two samples. In lung squamous tumors, it was highly expressed in one sample and moderately expressed in two others (n=13). Contig 47 was negative for 2/4 normal lung samples, with the remaining two samples having moderate expression. Also, Contig 47 showed moderate expression in large intestine, and pancreas, and low expression in skin, salivary gland, soft palate, stomach, bladder, resting PBMC, and tonsil.

Contig 48 (SEQ ID NO: 143) was expressed in all head and neck squamous cell tumors tested (17/17): highly expressed in 8/17 and moderately expressed in 7/17, with low expression in two samples. Expression levels in lung squamous tumors were high to moderate in three samples (n=13). Contig 48 was negative for one out of four normal lung samples, the remaining showing low or moderate expression. Contig 48 showed moderate expression in soft palate, large intestine, pancreas, and bladder, and low expression in esophagus, salivary gland, resting PBMC, and heart. Contig 49 (SEQ ID NO: 144) was

expressed at low to moderate levels in 6/17 head and neck squamous cell tumors tested. Expression levels in lung squamous tumors were moderate in three samples (n=13). Contig 49 was negative for 2/4 normal lung samples, the remaining samples showing low expression. Moderate expression levels in skin, salivary gland, large intestine, pancreas, bladder and resting PBMC were shown, as well as low expression in soft palate, lymph nodes, and tonsil. Contig 56 (SEQ ID NO: 148) was expressed in low to moderate levels in 3/17 head and neck squamous cell tumors tested, and in lung squamous tumors, showing low to moderate levels in three out of thirteen samples. Notably, low expression levels were detected in one adenocarcinoma lung tumor sample (n=2). Contig 56 was negative for 3/4 normal lung samples, and showed moderate expression levels in only large intestine, and low expression in salivary gland, soft palate, pancreas, bladder, and resting PBMC. Contig 58, also known as L769P, (SEQ ID NO: 150) was expressed at moderate levels in 11/17 head and neck squamous cell tumors tested and low expression in one additional sample. Expression in lung squamous tumors showed low to moderate levels in three out of thirteen samples. Contig 58 was negative for 3/4 normal lung samples, with one sample having low expression. Moderate expression levels in skin, large intestine, and resting PBMC were demonstrated, as well as low expression in salivary gland, soft palate, pancreas, and bladder. Contig 59 (SEQ ID NO: 157) was expressed in some head, neck, and lung squamous tumors. Low level expression of Contig 59 was also detected in salivary gland and large intestine.

Additionally, the full-length cDNA sequence for Contigs 22, referred to as L763P, is provided in SEQ ID NO: 158, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 159. Also, the full-length cDNA sequence incorporating Contigs 17, 19, and 24, referred to as L762P, is provided in SEQ ID NO: 160, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 161. Further analysis of L762P has determined it to be a type I membrane protein and two additional variants have been sequenced. Variant 1 (SEQ ID NO: 167 and the corresponding amino acid sequence in SEQ ID NO: 169) is an alternatively spliced form of SEQ ID NO: 160 resulting in deletion of 503 nucleotides, as well as deletion of a short segment of the expressed protein. Variant 2 (SEQ ID NO: 168 and the corresponding amino acid sequence

in SEQ ID NO: 170) has a two nucleotide deletion at the 3' coding region in comparison to SEQ ID NO: 160, resulting in a secreted form of the expressed protein.

The full-length cDNA sequence for contig 56 (SEQ ID NO: 148), referred to as L773P, is provided in SEQ ID NO: 171, with the predicted amino acid sequence in SEQ ID NO: 172. Subsequent Northern blot analysis of L773P demonstrates this transcript is differentially over-expressed in squamous tumors and detected at approximately 1.6 Kb in primary lung tumor tissue and approximately 1.3 Kb in primary head and neck tumor tissue.

Subsequent microarray analysis has shown Contig 58, also referred to as L769S (SEQ ID NO: 150), to be overexpressed in breast tumors in addition to lung squamous tumors.

Example 4

SYNTHESIS OF POLYPEPTIDES

Polypeptides may be synthesized on a Perkin Elmer/Applied Biosystems Division 430A peptide synthesizer using Fmoc chemistry with HPTU (O-Benzotriazole-N,N,N',N'-tetramethyluronium hexafluorophosphate) activation. A Gly-Cys-Gly sequence may be attached to the amino terminus of the peptide to provide a method of conjugation, binding to an immobilized surface, or labeling of the peptide. Cleavage of the peptides from the solid support may be carried out using the following cleavage mixture: trifluoroacetic acid:ethanedithiol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for 2 hours, the peptides may be precipitated in cold methyl-t-butyl-ether. The peptide pellets may then be dissolved in water containing 0.1% trifluoroacetic acid (TFA) and lyophilized prior to purification by C18 reverse phase HPLC. A gradient of 0%-60% acetonitrile (containing 0.1% TFA) in water (containing 0.1% TFA) may be used to elute the peptides. Following lyophilization of the pure fractions, the peptides may be characterized using electrospray or other types of mass spectrometry and by amino acid analysis.

From the foregoing, it will be appreciated that, although specific embodiments of the invention have been described herein for the purposes of illustration, various modifications may be made without deviating from the spirit and scope of the invention.

CLAIMS:

1. An isolated polynucleotide molecule comprising a nucleotide sequence selected from the group consisting of:
 - (a) sequences provided in SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168 and 171;
 - (b) the complements of sequences provided in SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168 and 171; and
 - (c) sequences that hybridize to a sequence of (a) or (b) under moderately stringent conditions.
2. An isolated polypeptide comprising an immunogenic portion of a lung tumor protein or a variant thereof, wherein said protein comprises an amino acid sequence encoded by a polynucleotide molecule of claim 1.
3. An isolated polynucleotide molecule comprising a nucleotide sequence encoding the polypeptide of claim 2.
4. An expression vector comprising an isolated polynucleotide molecule of claims 1 or 3.
5. A host cell transformed with the expression vector of claim 4.
6. The host cell of claim 5 wherein the host cell is selected from the group consisting of *E. coli*, yeast and mammalian cell lines.

7. A pharmaceutical composition comprising the polypeptide of claim 2 and a physiologically acceptable carrier.

8. A vaccine comprising the polypeptide of claim 2 and a non-specific immune response enhancer.

9. The vaccine of claim 8 wherein the non-specific immune response enhancer is an adjuvant.

10. A vaccine comprising an isolated polynucleotide molecule of claims 1 or 3 and a non-specific immune response enhancer.

11. The vaccine of claim 10 wherein the non-specific immune response enhancer is an adjuvant.

12. A pharmaceutical composition for the treatment of lung cancer comprising a polypeptide and a physiologically acceptable carrier, the polypeptide comprising an immunogenic portion of a lung protein or a variant thereof, wherein said protein comprises an amino acid sequence encoded by a polynucleotide molecule comprising a sequence selected from the group consisting of:

- (a) sequences recited in SEQ ID NO: 4, 5, 9, 14, 28, 31, 33, 50, 53, 56, 60, 70, 72, 75, 76, 79, 83, 85, 97-106, 115-124, 126, 130, 134-141, 143, 145-147 and 162-164;
- (b) sequences complementary to the sequences of SEQ ID NO: 4, 5, 9, 14, 28, 31, 33, 50, 53, 56, 60, 70, 72, 75, 76, 79, 83, 85, 97-106, 115-124, 126, 130, 134-141, 143, 145-147 and 162-164; and
- (c) sequences that hybridize to a sequence of (a) or (b) under moderately stringent conditions.

13. A vaccine for the treatment of lung cancer comprising a polypeptide and a non-specific immune response enhancer, said polypeptide comprising an immunogenic portion of a lung protein or a variant thereof, wherein said protein comprises an amino acid sequence encoded by a polynucleotide molecule comprising a sequence selected from the group consisting of:

- (a) sequences recited in SEQ ID NO: 4, 5, 9, 14, 28, 31, 33, 50, 53, 56, 60, 70, 72, 75, 76, 79, 83, 85, 97-106, 115-124, 126, 130, 134-141, 143, 145-147 and 162-164;
- (b) sequences complementary to the sequences of SEQ ID NO: 4, 5, 9, 14, 28, 31, 33, 50, 53, 56, 60, 70, 72, 75, 76, 79, 83, 85, 97-106, 115-124, 126, 130, 134-141, 143, 145-147 and 162-164; and
- (c) sequences that hybridize to a sequence of (a) or (b) under moderately stringent conditions.

14. A vaccine for the treatment of lung cancer comprising a DNA molecule and a non-specific immune response enhancer, the polynucleotide molecule comprising a sequence selected from the group consisting of:

- (a) sequences recited in SEQ ID NO: 4, 5, 9, 14, 28, 31, 33, 50, 53, 56, 60, 70, 72, 75, 76, 79, 83, 85, 97-106, 115-124, 126, 130, 134-141, 143, 145-147 and 162-164;
- (b) sequences complementary to the sequences of SEQ ID NO: 4, 5, 9, 14, 28, 31, 33, 50, 53, 56, 60, 70, 72, 75, 76, 79, 83, 85, 97-106, 115-124, 126, 130, 134-141, 143, 145-147 and 162-164; and
- (c) sequences that hybridize to a sequence of (a) or (b) under moderately stringent conditions.

15. A method for inhibiting the development of lung cancer in a patient, comprising administering to the patient an effective amount of the pharmaceutical composition of claims 7 or 12.

16. A method for inhibiting the development of lung cancer in a patient, comprising administering to the patient an effective amount of the vaccine of any one of claims 8, 10, 13 or 14.

17. A fusion protein comprising at least one polypeptide according to claim 2.

18. A fusion protein comprising a polypeptide according to claim 2 and a known lung tumor antigen.

19. A pharmaceutical composition comprising a fusion protein according to any one of claims 17-18 and a physiologically acceptable carrier.

20. A vaccine comprising a fusion protein according to any one of claims 17-18 and a non-specific immune response enhancer.

21. The vaccine of claim 20 wherein the non-specific immune response enhancer is an adjuvant.

22. A method for inhibiting the development of lung cancer in a patient, comprising administering to the patient an effective amount of the pharmaceutical composition of claim 19.

23. A method for inhibiting the development of lung cancer in a patient, comprising administering to the patient an effective amount of the vaccine of claim 20.

24. A method for detecting lung cancer in a patient, comprising:
(a) contacting a biological sample obtained from the patient with a binding agent which is capable of binding to a polypeptide, the polypeptide comprising an immunogenic portion of a lung protein or a variant thereof, wherein said protein comprises an amino acid sequence encoded by a polynucleotide molecule comprising a sequence selected

from the group consisting of nucleotide sequences recited in SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168 and 171 the complements of said nucleotide sequences and sequences that hybridize to a sequence of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168 and 171 under moderately stringent conditions; and

(b) detecting in the sample a protein or polypeptide that binds to the binding agent, thereby detecting lung cancer in the patient.

25. The method of claim 24 wherein the binding agent is a monoclonal antibody.

26. The method of claim 25 wherein the binding agent is a polyclonal antibody.

27. A method for monitoring the progression of lung cancer in a patient, comprising:

(a) contacting a biological sample obtained from the patient with a binding agent that is capable of binding to a polypeptide, said polypeptide comprising an immunogenic portion of a lung protein or a variant thereof, wherein said protein comprises an amino acid sequence encoded by a polynucleotide molecule comprising a sequence selected from the group consisting of nucleotide sequences recited in SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168 and 171 the complements of said nucleotide sequences and sequences that hybridize to a nucleotide sequence of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168 and 171 under moderately stringent conditions;

(b) determining in the sample an amount of a protein or polypeptide that binds to the binding agent;

(c) repeating steps (a) and (b); and

(d) comparing the amount of polypeptide detected in steps (b) and (c) to monitor the progression of lung cancer in the patient.

28. A monoclonal antibody that binds to a polypeptide comprising an immunogenic portion of a lung protein or a variant thereof, wherein said protein comprises an amino acid sequence encoded by a polynucleotide molecule comprising a sequence selected from the group consisting of: nucleotide sequences recited in SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168 and 171; the complements of said nucleotide sequences; and sequences that hybridize to a nucleotide sequence of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168 or 171 under moderately stringent conditions.

29. A method for inhibiting the development of lung cancer in a patient, comprising administering to the patient a therapeutically effective amount of a monoclonal antibody according to claim 28.

30. The method of claim 29 wherein the monoclonal antibody is conjugated to a therapeutic agent.

31. A method for detecting lung cancer in a patient comprising:

- (a) obtaining a biological sample from the patient;
- (b) contacting the sample with at least two oligonucleotide primers in a polymerase chain reaction, wherein at least one of the oligonucleotides is specific for a polynucleotide molecule encoding a polypeptide comprising an immunogenic portion of a lung protein or of a variant thereof, said protein comprising an amino acid sequence encoded by a polynucleotide molecule comprising a sequence selected from the group consisting of nucleotide sequences recited in SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168 and 171 the complements of said nucleotide sequences, and sequences that hybridize to a sequence of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168 or 171 under moderately stringent conditions; and

(c) detecting in the sample a polynucleotide sequence that amplifies in the presence of the oligonucleotide primers, thereby detecting lung cancer.

32. The method of claim 31, wherein at least one of the oligonucleotide primers comprises at least about 10 contiguous nucleotides of a polynucleotide molecule comprising a sequence selected from SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168 and 171.

33. A diagnostic kit comprising:

- (a) one or more monoclonal antibodies of claim 28; and
- (b) a detection reagent.

34. A diagnostic kit comprising:

- (a) one or more monoclonal antibodies that bind to a polypeptide encoded by a polynucleotide molecule comprising a nucleotide sequence selected from the group consisting of SEQ ID NO: 4, 5, 9, 14, 28, 31, 33, 50, 53, 56, 60, 70, 72, 75, 76, 79, 83, 85, 97-106, 115-124, 126, 130, 134-141, 143, 145-147 and 162-164 the complements of said sequences, and sequences that hybridize to a sequence of SEQ ID NO: 4, 5, 9, 14, 28, 31, 33, 50, 53, 56, 60, 70, 72, 75, 76, 79, 83, 85, 97-106, 115-124, 126, 130, 134-141, 143, 145-147 or 162-164 under moderately stringent conditions; and
- (b) a detection reagent.

35. The kit of claims 33 or 34 wherein the monoclonal antibodies are immobilized on a solid support.

36. The kit of claim 35 wherein the solid support comprises nitrocellulose, latex or a plastic material.

37. The kit of claims 33 or 34 wherein the detection reagent comprises a reporter group conjugated to a binding agent.

38. The kit of claim 37 wherein the binding agent is selected from the group consisting of anti-immunoglobulins, Protein G, Protein A and lectins.

39. The kit of claim 37 wherein the reporter group is selected from the group consisting of radioisotopes, fluorescent groups, luminescent groups, enzymes, biotin and dye particles.

40. A diagnostic kit comprising at least two oligonucleotide primers, at least one of the oligonucleotide primers being specific for a polynucleotide molecule encoding a polypeptide comprising an immunogenic portion of a lung protein or a variant thereof, said protein comprising an amino acid sequence encoded by a polynucleotide molecule comprising a sequence selected from the group consisting of nucleotide sequences recited in SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168 and 171 the complements of said nucleotide sequences and sequences that hybridize to a sequence of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168 or 171 under moderately stringent conditions.

41. A diagnostic kit of claim 40 wherein at least one of the oligonucleotide primers comprises at least about 10 contiguous nucleotides of a polynucleotide molecule comprising a sequence selected from SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168 and 171.

42. A method for detecting lung cancer in a patient, comprising:

- (a) obtaining a biological sample from the patient;
- (b) contacting the biological sample with an oligonucleotide probe specific for a polynucleotide molecule encoding a polypeptide comprising an immunogenic portion of a lung protein or a variant thereof, said protein comprising an amino acid sequence encoded by a polynucleotide molecule comprising a sequence selected from the group consisting of nucleotide sequences recited in SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168 and 171 the complements of said nucleotide sequences, and

sequences that hybridize to a sequence of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168 or 171 under moderately stringent conditions; and

(c) detecting in the sample a polynucleotide sequence that hybridizes to the oligonucleotide probe, thereby detecting lung cancer in the patient.

43. The method of claim 42 wherein the oligonucleotide probe comprises at least about 15 contiguous nucleotides of a polynucleotide molecule comprising a sequence selected from the group consisting of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168 and 171.

44. A diagnostic kit comprising an oligonucleotide probe specific for a polynucleotide molecule encoding a polypeptide comprising an immunogenic portion of a lung protein or a variant thereof, said protein comprising an amino acid sequence encoded by a polynucleotide molecule comprising a sequence selected from the group consisting of: nucleotide sequences recited in SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168 and 171; the complements of said nucleotide sequences; and sequences that hybridize to a sequence of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168 or 171 under moderately stringent conditions.

45. The diagnostic kit of claim 44, wherein the oligonucleotide probe comprises at least about 15 contiguous nucleotides of a polynucleotide molecule comprising a sequence selected from the group consisting of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168 and 171.

46. A method for treating lung cancer in a patient, comprising the steps of:

- (a) obtaining peripheral blood cells from the patient;
- (b) incubating the cells in the presence of at least one polypeptide of claim 2, such that T cells proliferate; and
- (c) administering to the patient the proliferated T cells.

47. A method for treating lung cancer in a patient, comprising the steps of:

- (a) obtaining peripheral blood cells from the patient;
- (b) incubating the cells in the presence of at least one polynucleotide of claim 1, such that T cells proliferate; and
- (c) administering to the patient the proliferated T cells.

48. The method of any one of claims 46 and 47 wherein the step of incubating the T cells is repeated one or more times.

49. The method of any one of claims 46 and 47 wherein step (a) further comprises separating T cells from the peripheral blood cells, and the cells incubated in step (b) are the T cells.

50. The method of any one of claims 46 and 47 wherein step (a) further comprises separating CD4+ cells or CD8+ cells from the peripheral blood cells, and the cells proliferated in step (b) are CD4+ or CD8+ T cells.

51. The method of any one of claims 46 and 47 wherein step (b) further comprises cloning one or more T cells that proliferated in the presence of the polypeptide.

52. A composition for the treatment of lung cancer in a patient, comprising T cells proliferated in the presence of a polypeptide of claim 2, in combination with a pharmaceutically acceptable carrier.

53. A composition for the treatment of lung cancer in a patient, comprising T cells proliferated in the presence of a polynucleotide of claim 1, in combination with a pharmaceutically acceptable carrier.

54. A method for treating lung cancer in a patient, comprising the steps of:

- (a) incubating antigen presenting cells in the presence of at least one polypeptide of claim 2;

(b) administering to the patient the incubated antigen presenting cells.

55. A method for treating lung cancer in a patient, comprising the steps of:

(a) incubating antigen presenting cells in the presence of at least one polynucleotide of claim 1;

(b) administering to the patient the incubated antigen presenting cells.

56. The method of claims 54 or 55 wherein the antigen presenting cells are selected from the group consisting of dendritic cells and macrophage cells.

57. A composition for the treatment of lung cancer in a patient, comprising antigen presenting cells incubated in the presence of a polypeptide of claim 2, in combination with a pharmaceutically acceptable carrier.

58. A composition for the treatment of lung cancer in a patient, comprising antigen presenting cells incubated in the presence of a polynucleotide of claim 1, in combination with a pharmaceutically acceptable carrier.

SEQUENCE LISTING

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 gacaacctac tttgcttggc tgaagtgaag aatgatattc atatnttcat ttattccatg 360
 gacatttagt tagtgctttt tatataccag gcatgatgct gagtgcacct ctttgtgata 420
 tntccaaatn ttngtncngt cgctgcacat atctgaaatc ctatattaag antttcccaa 480
 natgangtcc ctgggttttc cagccactt gatcngtcaa ngatctcacc tctgtntgtc 540
 ctaaaacnt ctntnnang gttagacngg acctctctc ccccttcccg aanaatnaag 600
 tgtgrgaaga nannccnncn ccccccncn tcnncctng cngctnnnc cncntgtngg 660

ggngngccgcc cccgcggggg gacccccccn ttttcccc

698

<210> 6
 <211> 740
 <212> DNA
 <213> Homo sapien
 <220>
 <221> misc_feature
 <222> (1)...(740)
 <223> n = A,T,C or G

<400> 6
 actagtcaaa aatgctaaaa taatttggga gaaaatattt ttttaagtagt gttatagttt 60
 catgtttatc ttttattatg tnttgtgaag ttgtgtcttt tcactaatta cctatactat 120
 gccaatattt ccttatatct atccataaca tttatactac attctgtaaga gaatatgcac 180
 gtgaaacrta acactttata aggtaaaaat gaggtttcca agatttaata atctgatcaa 240
 gttcttgta tttccaaata gaatggactt ggtctgttaa ggggctaagg gagaagaaga 300
 agataagggt aaaagttgtt aatgaccaaa catttctaaaa gaaatgcaaa aaaaaattta 360
 ttttcaagcc ttcaactat ttaaggaaaag caaaatcatt tccttanatgc atatcatctg 420
 tgagantttc tcantaatat cctgaatcat tcatttcagc tnaggcttca tgttgactcg 480
 atatgtcatc tagggaaaagt ctatttcatt gtccaaacct gttgccatag ttggttaggc 540
 tttcttttaa ntgtgaanta ttnacangaa attttctctt tnanagttct tnatagggtt 600
 aggggtgtgg gaaaagcttc taacaatctg tagtgctncg tgttatctgt ncagaaccan 660
 aatnacggat cgnangaagg actgggtcta tttacangaa cgaatnatct ngtnnnctgt 720
 gtnnncaact cngggagcc 740

<210> 7
 <211> 670
 <212> DNA
 <213> Homo sapien
 <220>
 <221> misc_feature
 <222> (1)...(670)
 <223> n = A,T,C or G

<400> 7
 gctggggagc tcggcatggc ggtccccgct gcagccatgg ggccctcggc gttggggcag 60
 agcggccccc gctcgatggc cccgtggtgc tcagttagca gcggcccgct gcgctacgtg 120
 cttgggatgc aggagctggt ccggggccac agcaagaccg cgagtctctg gcgcacagcg 180
 ccaagggtgca ctccgtggcc tggagttgct acgggcgtcg cctacctcgg ggtcttcgac 240
 aagacgccac gtcttcttgc tgganaanga ccgttggtca aagaaaacaa ttatcgggga 300
 catggggata gtgtggacca ctttgttggc atccaagtaa tcctgacctt ttgtttacgg 360
 cgtctggaga taaaaccatt cgcattctgg atgtgaggac tacaaaatgc attgccactg 420
 tgaacactaa aggggagaaac attaatatct gctggantcc tgatgggcan accattgctg 480
 tagcnacaag gatgatgtcg tgactttatt gatgccaaga aacccccgtc caaagcaaaa 540
 aaacanttcc aanttcgaag tcaccnaaat ctcttgggac aatgaacatn aatatntctt 600
 tcctgacaat ggnccctggg tgnctcacat cctcagctnc cccaaaactg aancctgtnc 660
 natccacccc 670

<210> 8
 <211> 689
 <212> DNA
 <213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(689)
<223> n = A,T,C or G

<400> 8

actagatctt	aggaatgaac	agtaaaagag	gagcagttgg	ctacttgatt	acaacagagt	60
aaatgaagta	ctggatttgg	gaaaacctgg	ttttattaga	acatatggaa	tgaaagccta	120
cacctagcat	tgccacttta	gccccctgaa	ttaacagagc	ccaattgaga	caaaccctcg	180
gcaacaggaa	attcaaggga	gaaaaagtaa	gcaacttggg	ctaggatgag	ctgactccct	240
tagagcaaaag	ganagacagc	ccccattacc	aaataccatt	tttgcctggg	gcttgtgcag	300
ctggcagtg	tcctgcccc	gcatggcacc	ttatngtttt	gatagcaact	tcgttgaatt	360
ttcaccaact	tattacttga	aattataata	tagcctgtcc	gtttgcgtgn	tcagggtgt	420
gatatacttt	cctagtgggt	tgacttttaa	aataaatnag	gtttantttt	ctcccccn	480
cnntnctncc	nntnctenn	cnntcccccc	cnctengtcc	tcnnnnntn	gggggggccc	540
ccccnccggn	ggacccccct	ttggtccctt	agtggagggt	natggcccc	ggnnttatcc	600
nggccttann	tttccccgtn	nnaaatgntt	ccccctccca	ntcccnccac	ctcaancogg	660
aagcctaagt	ttntaccctg	gggggtcccc				689

<210> 9
<211> 674
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(674)
<223> n = A,T,C or G

<400> 9

gtccactctc	ctttgagtg	actgtcttac	tgtgcactct	gtttttcaac	tttctagata	60
taaaaaatgc	ttgttctata	gtggagtaag	agctcacaca	cccaaggcag	caagataact	120
gaaaaaagcg	aggctttttt	gccaccttgg	taaaggccag	ttcactgcta	tagaactgct	180
ataagcctga	aggggaagtag	ctatgagact	ttccattttt	cttagttctc	ccaataggct	240
ccttcatgga	aaaaggcttc	ctgtaataat	tttcacctaa	tgaattagca	gtgtgattat	300
ttctgaaata	agagacaaat	tgggccgcag	agtcttcctg	tgatttaaaa	taaacaaccc	360
aaagttttgt	ttggtcttca	ccaaaggaca	tactctaggg	gggtatgtgt	tgaagacatt	420
caaaaacatt	agctgttctg	tctttcaatt	tcaagttatt	ttggagactg	cctccatgtg	480
agttaattac	tttgctctgg	aactagcatt	attgtcatta	tcatcacatt	ctgtcatcat	540
catctgaata	atattgtgga	tttccccctc	tgcttgcata	ttcttttgac	tcctctggga	600
anaaatgtca	aaaaaaaagg	tcgatctact	cngcaaggnc	catctaata	ctgcgctgga	660
aggaccnct	gccc					674

<210> 10
<211> 346
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(346)
<223> n = A,T,C or G

<400> 10

<221> misc_feature
 <222> (1)...(694)
 <223> n = A,T,C or G

<400> 13
 cactagtcac tcattagcgt tttcaatagg gctcttaagt ccagtagatt acgggtagtc 60
 agttgacgaa gatctgggtt acaagaacta attaaatgtt tcattgcatt tttgtaagaa 120
 cagaataatt ttataaaatg tttgtagttt ataattgccg aaaataattt aaagacactt 180
 tttctctgtg tgtgcaaagt tgtgtttgtg atccattttt tttttttttt taggacacct 240
 gtttactagc tagctttaca atatgccaaa aaaggatttc tccctgacct catccgtggg 300
 tcacctctt tcccccccat gctttttgcc ctagtattata acaaagggaat gatgatgatt 360
 taaaaagtag ttctgtatct tcagtatctt ggtcttccag aacctctctg ttgggaaggg 420
 gatcattttt tactgggtcat ttccctttgg agtgactac tttaacagat ggaaagaact 480
 cattggccat ggaaacagcc gangtggtg gagccagcag tgcattggac cgtccggcat 540
 ctggcctgat tggctgggt gccgtcattg tcagcacagt gccatgggac atggggaana 600
 ctgactgcac ngccaatggt tttcatgaag aatacngcat ncnngtgat cactgnancc 660
 angacgctat gggggncana gggccanttg ctcc 694

<210> 14
 <211> 679
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(679)
 <223> n = A,T,C or G

<400> 14
 cagccgcctg catctgtatc cagcgccang tcccgccagt cccagctgcg cgcgcccccc 60
 agtcccgnc cgttcggcc cangtcnagt tagnctcac catnccggtc aaaggangca 120
 ccaagtgcac caaataacct cngtnccgat ntaaatccat ctctctggct gccgggattg 180
 ctgtccntgc cattggacta nggtccgat negactctca gaccanganc atcttcganc 240
 naganactaa tnatnattnt tccagcttct acacaggagt ctatattctg atcggatccg 300
 gcnccctent gatgctggtg ggcttcctga gctgctgagg ggctgtgcaa gagtcccant 360
 gcatgctggg actgttcttc ggcttcntct tggatgatn cgccattgaa atacctgagg 420
 ccattctggg atattccact ncgatnatgt gattaaggaa ntccacggag ttttacaagg 480
 acacgtacaa cnacctgaaa accnnggatg anccccaccg ggaancnctg aangccatcc 540
 actatgcgtt gaactgcaat ggtttggctg gggnccttga acaatttaat cncatacatc 600
 tggccccann aaaggacntn ctcganncc tcnccgtgna attcngttct gatnccatca 660
 cagaagtctc gaacaatcc 679

<210> 15
 <211> 695
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(695)
 <223> n = A,T,C or G

<400> 15
 actagtggat aaaggccagg gatgctgctc aacctcctac catgtacagg gacgtctccc 60
 cattacaact acccaatccg aagtgtcaac tgcgtcagga ctaanaaac ctggctctga 120

```

actagtctgc tgatagaaa cactatacat cctattgttt ctttctttcc aaaatcagcc      60
ttctgtctgt aacaaaaatg tactttatag agatggagga aaaggtctaa tactacatag      120
ccttaagtgt ttctgtcatt gttcaagtgt attttctgta acagaaacat atttggaatg      180
tttttctttt ccccttataa attgtaattc ctgaaatact gctgctttaa aaagtccac      240
tgtcagatta tattatctaa caattgaata ttgtaaatat acttgtctta cctctcaata      300
aaagggtact ttctatttan nnagnngnnn gnnnnataaa anaaaaa      346

```

```

<210> 11
<211> 602
<212> DNA
<213> Homo sapien

```

```

<400> 11
actagtaaaa agcagcattg ccaaataatc cctaattttc cactaaaaat ataatgaaat      60
gatgttaagc tttttgaaaa gttaggttta aacctactgt tgtagatta atgtatttgt      120
tgcttccttt tatctggaat gtggcattag cttttttatt ttaacctctt ttaattctta      180
ttcaattcca tgacttaagg ttggagagct aaacactggg atttttggat aacagactga      240
cagttttgca taattataat cggcattgta catagaaaagg atatggctac cttttgttaa      300
atctgcactt tctaaatata aaaaaaggga aatgaagtta taaatcaatt tttgtataat      360
ctgtttgaaa catgagtttt atttgcttaa cattagggct ttgccccctt tctgtaagtc      420
tcttgggact ctgtgtagaa ctgttctcat taaacaccaa acagttaagt ccattctctg      480
gtactagcta caaattcggg ttcataattct accttaacaat ttaataaac tgaaatattt      540
ctagatgggt tacttctgtt catataaaaa caaaacttga ttccaaaaa aaaaaaaaaa      600
aa                                     602

```

```

<210> 12
<211> 685
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(685)
<223> n = A,T,C or G

```

```

<400> 12
actagtcctg tgaaagtaca actgaaggca gaaagtgtta ggatttttga tctaagtctc      60
attatcatgg tattgatgga cctaagaaaa taaaaattag actaagcccc caaataagct      120
gcatgcattt gtaacatgat tagtagattt gaatatatag atgtagtatn ttgggtatct      180
agggtcttta tcattatgta aaggaattaa agtaaaggac tttgtagtgt tttttattaa      240
atatgcatat agtagagtgc aaaaatatag caaaaatana aactaaaggc agaaaagcat      300
tttagatatg ccttaatnta nnaactgtgc caggtggccc tcggaataga tgccaggcag      360
agaccagtgc ctgggtgggt cctccccctg tctgcccccc tgaagaactt cctcacgtg      420
angtagtgcc ctctgagggt tcacgtggan tantggganc aggccgnncn gtnanaagaa      480
ancanngtga nagtttcncc gtngangcng aactgtccct gngccnnnac gctcccanaa      540
cntntccaat ngacaatcga gtttcnnnc ttcngnaacc tngccgnnnn cngcccnnc      600
cantntgnta accccgcgcc cggatcgctt tcnnttcgtt ctcnncncaa ngggntttcn      660
cnncgcctgt cncnnccccg cnncc                                     685

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```

<210> 13
<211> 694
<212> DNA
<213> Homo sapien

```

```

<220>

```

```

ttaaaaaagg gcttgaaaaa aggggagcca caaatctgtc tgcttcctca cnttantcnt 180
tggcaaatna gcattctgtc tcnttggtcg cngcctcanc ncaaaaaanc ngaactcnat 240
cngggccagg aatacatctc ncaatnaacn aaattganca aggcnnntggg aaatgccnga 300
tgggattatc ntccgcttgt tgancctcta agtttcttcc ccttcattcn accctgccag 360
ccnagtctcg tttagaaaaat gccngaattc naacnccggt tttctactc ngaatttaga 420
tctncanaaa ctctctggcc acnattcnaa ttannggnca cgnacanatn ccttccatna 480
ancncacccc acntttgana gccangacaa tgactgcntn aantgaaggc ntgaaggaaan 540
aactttgaaa ggaaaaaaa ctttgtttcc ggccccttcc aacncttctg tgttnancac 600
tgcccttctng naacctctga agcccnngna cagtgttaca tgttgttcta nnaaacngac 660
ncttnaatnt cnatcttccc nanaacgatt ncnc 695

```

```

<210> 16
<211> 669
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(669)
<223> n = A,T,C or G

```

```

<400> 16
cgccgaagca gcagcgcagg ttgtcccggt ttcccccctcc ccttcccctc tccgggttgc 60
ttcccgggcc ccttacactc cacagtcccg gtcccgccat gtcccagaaa caagaagaag 120
agaacccctgc ggaggagacc ggcgaggaga agcaggacac gcaggagaaa gaaggtattc 180
tgcttgagag agctgaagag gcaaagctaa aggcctaaata cccaagccta ggacaaaagc 240
ctggaggctc cgacttcttc atgaagagac tccagaaaagg gcaaaaagtac tttgactcng 300
gagactacaa catggccaaa gccaacatga agaataagca gctgccaaagt gcangaccag 360
acaagaacct ggtgactggt gatcacatcc ccaccccaca ggatctgcc agagaaagtc 420
ctcgtctgtc accagcaagc ttgcgggtgg ccaagttgaa tgatgctgcc ggggctctgc 480
canatctgag acgcttccct ccttgcctcc cccgggtcct gtgctggctc ctgccccttc 540
tgcttttgca gccangggtc aggaagtggc ncnggtngtg gctggaaagc aaaaccttct 600
cctgttggcg tcccacccat ggagccctcg gggcgagccc angaacttga ncccttctgt 660
tntcttnc 669

```

```

<210> 17
<211> 697
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(697)
<223> n = A,T,C or G

```

```

<400> 17
gcaagatatg gacaactaag tgagaaggta atnctctact gctctagntn ctcnngcnn 60
gacgcgctga ggagannnac gctggcccan ctgcgggcca cacacgggga tcntggtnat 120
gcttgcccan gggancccca ncncctcgan ccatntcac acccgnncn tncgcccacn 180
ncttgctcn cncngccng nccagctcnc gncccccctc gccnnnctcn ttncnctctc 240
cncnccctc ncnaacnct cctaccncng gctccctccc cagccccccc ccgcaancct 300
ccacnacnc ncrnncng anncnctc gcnctcngcc cncgcccct gcccccgc 360
cncnacnnc cgnctccccc cgcncgngc ctnccccc ccaacnacag ncnaccgc 420
agnacgcnc tccgcccnc gacgcccnn ccgcccgcgc tcacctcat ggnccnang 480
cccgctcnc nccnctgnc gcgncnng cgcggcgcc cnnccngntn ccnccngng 540

```

```

ccccngcngn angcngtgcg cnncangncc gngccggnnn ncaccctccg nccnccgccc 600
cgcccgcgtgg gggctccccgc cncgcggntc antcccccnc cntncgcccc ctntccgntc 660
cnnncntcnc gctcngcgcn cgcccnccnc cccccc 697

```

```

<210> 18
<211> 670
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (670)
<223> n = A,T,C or G

```

```

<400> 18
ctcgtgtgaa gggctgcagta cctaagccgg agcggggtag aggcggggcg gcacccccct 60
ctgacctcca gtgccgcccgg cctcaagatc agacatggcc cagaacttga acgacttgcc 120
gggacggctg cccgccgggc cccggggcat gggcacggcc ctgaagctgt tgctgggggc 180
cgccgccttg gccctacggtg tgcgcgaatc tgggttcacc gtggaaggcg ggncagagc 240
catctctctc aatcggatcg gtggagtga caggacacta tccctgggccc anggccttca 300
cttcaggatc cttgggtcca gtacccanc atctatgaca ttcggggccag acctcgaaaa 360
aatctctctc ctacaggctc caaagaccta cagatggtga atatctccct gcgagtgttg 420
tctcgaccaa tgctcangaa ctccctaaca tggtccancg cctaagggct ggactacnaa 480
gaacgantgt tgcggtccat tgccacgaag tgctcaagaa tttnggtggc caagttcaat 540
gncctcacnn ctgactncctc agcggggcca agttanccct gggtgatccc cgggganctg 600
acnnaaaagg gccaaaggact tccctctatc ctggataatg tggccttcac aaagctcaac 660
tttancacc 670

```

```

<210> 19
<211> 606
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (606)
<223> n = A,T,C or G

```

```

<400> 19
actagtgcc aacctagctc ccaggccagt tctctgaatg tcgaggagtt ccaggatctc 60
tggcctcagt tgtccttggg tattgatggg ggacaaattg gggatggcca gagccccgag 120
tgtcgcttgg gctcaactgt gggtgatatt tctgtgcccg gaaagtgttg catcattcgt 180
ccaggctgtg ccttggaag tactacagcc atcctccaac agaagtacgg actgctcccc 240
tcacatgcgt cctacctgtg aaactctggg aagcaggaag gcccaagacc tgggtgctgga 300
tactatgtgt ctgtccactg acgactgtca aggcctcatt tgcagaggcc accggagcta 360
gggcactagc ctgactttta aggcagtgtg tctttctgag cactgtagac caagcccttg 420
gagctgctgg tttagccttg cacctgggga aaggatgtat ttatttgat tttcatatat 480
cagccaaaag ctgaatggaa aagttnagaa cattcctagg tggccttatt ctaataagtt 540
tctctgtctt gttttgtttt tcaattgaaa agttattaaa taacagattt agaatttagt 600
gagacc 606

```

```

<210> 20
<211> 449
<212> DNA
<213> Homo sapien

```

```

<400> 20
actagtaaac aacagcagca gaaacatcag tatcagcagc gtcgccagca ggagaatatg      60
cagcgccaga gccgaggaga acccccgctc cctgaggagg acctgtccaa actcttcaaa      120
ccaccacagc cgcctgccag gatggactcg ctgctcattg caggccagat aaacacttac      180
tgccagaaca tcaaggagtt cactgcccac aacttaggca agctcttcat ggcccaggct      240
cttcaagaat acaacaacta agaaaaggaa gtttccagaa aagaagttaa catgaactct      300
tgaagtcaca ccagggaac tcttggaaag aatatatttg catattgaaa agcacagagg      360
atttcttttag tgtcattgcc gattttggct ataacagtgt ctttctagcc ataataaaat      420
aaaacaaaat cttgactgct tgctcaaaa      449

<210> 21
<211> 409
<212> DNA
<213> Homo sapien

<400> 21
tatcaatcaa ctggtgaata attaaacaat gtgtgggtgtg atcatacaaa gggtaggact      60
caatgataaa aggaacaagc tgcctatatg tggacaaca tggatgcatt tcagaaactt      120
tatgttgagt gaaagaacaa acacggagaa catactatgt ggttctcttt atgtaacatt      180
acagaaataa aaacagaggc aaccaccttt gaggcagtat ggagtggagt agactggaaa      240
aagggaaggaa ggaacttcta cgtgatgga aatgtctgtg tcttcattgg gtggtagtta      300
tgtggggata tacatttgtc aaaatttatt gaactatata ctaaaagaact ctgcatttta      360
ttgggatgta aataatacct caattaaaaa gacaaaaaaa aaaaaaaaaa      409

<210> 22
<211> 649
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(649)
<223> n = A,T,C or G

<400> 22
acaattttca ttatcttaag cacattgtac atttctacag aacctgtgat tattctcgca      60
tgataaggat ggtacttgca tatggtgaat tactactgtt gacagtttcc gcagaaatcc      120
tatttcagtg gaccaacatt gtggcatggc agcaaatgcc aacattttgt ggaatagcag      180
caaactctaca agagaccctg gtgggttttt cgttttgttt tctttgtttt ttcccccttc      240
tcctgaatca gcagggatgg aangagggtta gggaagttaa gaattactcc ttccagtagt      300
agctctgaag tgtcacattt aatatcagtt ttttttaaac atgattctag tttaatgtag      360
aagagagaag aaagaggaag tgttcacttt tttaatacac tgatttagaa atttgatgtc      420
ttatatcagt agtcttgagg tattgatagc ctgctttatt tctgccttta cgttgacagt      480
gttgaagcag ggtgaataac taggggcata tatatttttt ttttttgtaa gctgtttcat      540
gatgttttct ttggaatttc cggataagtt caggaaaaca tctgcattgt gttatctagt      600
ctgaagttnn tatccatctc attacaacaa aaacnccag aacggnntg      649

<210> 23
<211> 669
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature

```


<222> (1)...(669)

<223> n = A,T,C or G

<400> 23

actagtgccg	tactggctga	aatccctgca	ggaccaggaa	gagaaccagt	tcagactttg	60
tactctcagt	caccagctct	ggaattagat	aaattccttg	aagatgtcag	gaatgggac	120
tatcctctga	cagcctttgg	gctgcctcgg	ccccagcagc	cacagcagga	ggaggtgaca	180
tcacctgtcg	tgcccccttc	tgtcaagact	ccgacacctg	aaccagctga	ggtggagact	240
cgcaagggtg	tgctgatgca	gtgcaacatt	gagtcgggtg	aggagggagt	caaacaccac	300
ctgacacttc	tgctgaagtt	ggaggacaaa	ctgaaccggc	acctgagctg	tgacctgatg	360
ccaaatgaga	atatccccga	gttggcgggc	gagctgggtg	agctgggctt	cattagttag	420
gctgaccaga	gccggttgac	ttctctgcta	gaagagactt	gaacaagttc	aattttgcca	480
ggaacagtac	cctcaactca	gccgctgtca	ccgtctcttc	ttagagctca	ctcggggccag	540
gcctgtatct	gcgctgtggc	tgtcctggac	gtgctgcacc	ctctgtcttc	ccccccagtc	600
agtattacct	gtgaagccct	tcctctcttc	attattcagg	anggctgggg	gggctccttg	660
nttctaacc						669

<210> 24

<211> 442

<212> DNA

<213> Homo sapien

<400> 24

actagtacca	tcttgacaga	ggatacatgc	ccccaaaacg	tttgttacca	cacttaaaaa	60
tcactgccat	cattaagcat	cagtttcaaa	attatagcca	ttcatgatct	actttttcca	120
gatgactatc	attattctag	tcctttgaat	ttgtaagggg	aaaaaaaaa	aaaacaaaaa	180
cttacgatgc	acttttcttc	agcacatcag	atttcaaatc	gaaaattaaa	gacatgctat	240
ggtaatgcac	ttgctagtac	tacacacttt	ggtacaacaa	aaaacagagg	caagaaacaa	300
cggaaagaga	aaagccttcc	tttgttggcc	cttaaaactg	gtcaagatct	gaaatgtaga	360
gatgatctct	gacgatacct	gtatgttctt	atttgtgtaa	taaaattgct	ggtagaaat	420
gacctaaaaa	aaaaaaaaa	aa				442

<210> 25

<211> 656

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(656)

<223> n = A,T,C or G

<400> 25

tgcaagtacc	acacactggt	tgaattttgc	acaaaaagtg	actgtaggat	caggtgatag	60
ccccggaatg	tacagtgtct	tgggtgcacca	agatgccttc	taaaggctga	cataccttgg	120
accctaattg	ggcagagagt	atagccctag	cccagtggcg	acatgaccac	tccctttggg	180
aggcctgagg	tagaggggag	tggtagtgtt	tttctcagtg	gaagcagcac	atgagtgggt	240
gacaggatgt	tagataaagg	ctctagtttag	ggtgtcattg	tcatttgaga	gactgacaca	300
ctcctagcag	ctggtaaaag	ggtgctggan	gccatggagg	anctctagaa	acattagcat	360
gggctgatct	gattacttcc	tggcatcccg	ctcactttta	tgggaagtct	tattagangg	420
atgggacagt	tttccatata	cttgcctgtg	agctctggaa	cactctctaa	atttccctct	480
attaaaaatc	actgcctctaa	ctacacttcc	tccttgaaag	aatagaaatg	gaactttctc	540
tgacatannt	cttgccatgg	ggagccagcc	acaaatgana	atctgaacgt	gtccaggttt	600
ctcctganac	tcattctacat	agaattgggt	aaaccctccc	tcggaataag	gaaaaa	656

11

<210> 26
 <211> 434
 <212> DNA
 <213> Homo sapien

 <220>
 <221> misc_feature
 <222> (1)...(434)
 <223> n = A,T,C or G

<400> 26
 actagtccag actgccacgc caaccccaga aaatacccca catgccagaa aagtgaagtc 60
 ctaggtgttt ccatctatgt ttcaatctgt ccatctacca ggctcgcga taaaaacaaa 120
 acaaaaaaac gctgccaggt tttagaagca gtctcgggtc caaaaccatc aggatcctgc 180
 caccaggggt cttttgaaat agtaccacat gtaaaaggga atttggcttt cacttcacct 240
 aataactgaa ttgtcaggct ttgattgata attgtagaaa taagttagcct tctgttgagg 300
 gaataagtta taatcagtat tcatctcttc gtcttttctc actcttttct ctctaattgt 360
 gtcattcgtc ctgtttgaaa aatatttctt ctatnaaatt aaactaacct gccttaaaaa 420
 aaaaaaaaaa aaaa 434

<210> 27
 <211> 654
 <212> DNA
 <213> Homo sapien

 <220>
 <221> misc_feature
 <222> (1)...(654)
 <223> n = A,T,C or G

<400> 27
 actagtccaa cacagtcaga aacattgttt tgaatcctct gtaaaccaag gcattaatct 60
 taataaaacca ggatccatct aggtaccact tgatataaaa aggatatcca taatgaatat 120
 cttataactgc atcctttaca ttagccacta aatacgttat tgcttgatga agacctttca 180
 cagaatccta tggattgcag catttcactt ggctacttca taccatgccc ttaaagaggg 240
 gcagtttctc aaaagcagaa acatgccgcc agttctcaag ttttctctct aactccattt 300
 gaatgtaagg gcagctggcc cccaatgtgg ggaggtcga acattttctg aattccattt 360
 ttcttgttcg cggctaaatg acagtttctg tcattactta gattccgac tttcccaaaag 420
 gtgttgattt acaaagaggc cagctaatag cagaaatcat gacctgaaa gagagatgaa 480
 attcaagctg tgagccaggc agganctcag tatggcaaag gtcttgagaa tcngccattt 540
 ggtacaaaaa aaattttaaa gcntttatgt tataccatgg aaccatagaa anggcaaggg 600
 aattgttaag aanaatttta agtgtccaga cccanaanga aaaaaaaaaa aaaa 654

<210> 28
 <211> 670
 <212> DNA
 <213> Homo sapien

 <220>
 <221> misc_feature
 <222> (1)...(670)
 <223> n = A,T,C or G

<400> 28
 cgtgtgcaca tactgggagg atttccacag ctgcacggtc acagccctta cggattgcca 60

```

ggaaggggcg aaagatatgt gggataaaact gagaaaagaa nccaaaaacc tcaacatcca 120
aggcagctta ttcgaactct gcggcagcgg caacggggcg gcgggggtccc tgctcccggc 180
gttcccgggtg ctctctggtgt ctctctcggc agcttttagcg acctgncctt cctctctgagc 240
gtggggccag cccccccgc gcgcccacc cacnctcact ccatgctccc ggaaatcgag 300
aggaagatca ttagttcttt ggggacgttn gtgattctct gtgatgctga aaaacactca 360
tatagggaac gtgggaaatc ctganctctt tnttatntcg tntgatttct tgtgttttat 420
ttgccaaaat gttaccaatc agtgaccaac cnagcacagc caaaaatcgg acntcngctt 480
tagtccgtct tcacacacag aataagaaaa cggcaaacc accccacttt tnanttttat 540
tattactaan ttttttctgt tgggcaaaag aatctcagga acngccctgg ggcnccgta 600
ctanagttaa ccnagctagt tncatgaaaa atgatgggct ccnctcaat gggaagcca 660
agaaaaagnc
670

```

```

<210> 29
<211> 551
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(551)
<223> n = A,T,C or G

```

```

<400> 29
actagtcttc cacagcctgt gaatccccct agacctttca agcatagtga gcggagaaga 60
agatcttcagc gtttagccac cttaacctatg cctgatgatt ctgtagaaaa ggttctcttc 120
ccctctccag ccaatgatgg gaaagtattc tccatcagtt ctcaaaatca gcaagaatct 180
tcagtaccag aggtgcctga tgttgccacac ttgccacttg agaagctggg acctgtctc 240
cctcttgact taagtcgtgg ttccagaagtt acagcaccgg tagcctcaga tctctcttac 300
cgtaatgaat gtcccaggggc agaaaaagag gatacncaga tgcttccaaa tcttctcttc 360
aaagcaatag ctgatgggaa gaggagctcc agcagcagca ggaacatcga aaacagaaaa 420
aaaaagtgaat ttgggaagac aaaagctcaa cagcatttgg taaggagaaa aganaagatg 480
aggaaggaag agagaagaga gacnaagatc nctacggacc gnnncggaag aagaagaagn 540
aaaaanaaa a
551

```

```

<210> 30
<211> 684
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(684)
<223> n = A,T,C or G

```

```

<400> 30
actagttcta tctggaaaaa gcccggttg gaagaagctg tggagagtgc gtgtgcaatg 60
cgagactcat tcttgggaag catccctggc aaaaatgcag ctgagtacaa ggttatcact 120
gtgatagaac ctggactgct ttttgagata atagagatgc tgcagctctga agagacttcc 180
agcacctctc agttgaatga attaatgatg gcttctgagt caactttact ggctcaggaa 240
ccacgagaga tgactgcaga tgaatcagag cttaaaaggga aattcctcat caacttagaa 300
ggtcgttgata ttctggaaga gtcttcttat aaagtaattg tcatgccgac tacgaaagaa 360
aaatgccccg gttgttgga gatacagcg ggagtcttca gatacactgc gtctctgatg 420
tcgagaagtt gtcagtggga aaatagtatt aacagctcac tcgagcaaga accctctga 480
cagtactggg ctagaagttt ggatggatta tttacaatat aggaagaaa gccaaagaa 540
aggtnatgag tggatgagta aatgggtggan gatggggaat tcaaatcaga attatggaag 600

```

aagtntttcc tgttactata gaaaggaatt atgtttatctt acatgcagaa aatatanatg 660
 tgtgggtgtgt accgtggatg gaan 684

<210> 31
 <211> 654
 <212> DNA
 <213> Homo sapien
 <220>
 <221> misc_feature
 <222> (1)...(654)
 <223> n = A,T,C or G

<400> 31
 gcgcagaaaa ggaaccaata tttcagaaac aagcttaata ggaacagctg cctgtacatc 60
 aacatcttct cagaatgacc cagaagttat catcgtggga gctggcgtgc ttggctctgc 120
 ttggcagct gtgctttcca gagatggaag aaaggcgaca gtcattgaga gagacttaaa 180
 agagcctgac agaatagtgt gagaattctt gcagccgggt gggtatcatg ttctcaaaga 240
 ccttggtctt ggagatacag tgaaggtctt tgatgccag gttgtaaatg gttacatgat 300
 tcatgatcag ggaagcaaaa tcagangtct agattcctta cctctgtgca gaaaacaatc 360
 aagtgcagag tgaagagctt ttccatcacg gaagattcat catgagtcct cggaaagcag 420
 ctatggcaga gcccaatgca aagtttattg aagggtgtgt gttacagtta ttagaggaaag 480
 atgatgttgt gatgggagt cagtacaagg ataaagagac tgggagatat caaggaaactc 540
 catgctccac tgactgttgt tgcagatggg tttttctcca anttcaggaa aagcctggctc 600
 tcaataaagt ttctgtatca ctcatcttgg tggcttctta tgaagaatgc nccc 654

<210> 32
 <211> 673
 <212> DNA
 <213> Homo sapien
 <220>
 <221> misc_feature
 <222> (1)...(673)
 <223> n = A,T,C or G

<400> 32
 actagtgaag aaaaagaaat tctgatacgg gacaaaaatg ctcttcaaaa catcattctt 60
 tatcacctga caccaggagt tttcatttga aaaggatttg aacctgggtg tactaacatt 120
 ttaagacca cacaagggaag caaaatcttt ctgaaagaag taaatgatac acttctggtg 180
 aatgaattga aatcaaaaaga atctgacatc atgacaacaa atgggtgtaat tcatgttcta 240
 gataaactcc tctatccagc agacacacct gtgggaaatg atcaactgct ggaaatactt 300
 aataaattaa tcaaatacat ccaaattaag ttgttctgtg gtagcacctt caaagaaatc 360
 cccgtgactg tctatnagcc aattattaaa aaatacacca aaatcattga tgggagtgcc 420
 tgtgggaaat aactgaaaaa gagaccgaga agaacgaatc attacaggtc ctgaaataaa 480
 atacctagga tttctactgg aggtggagaa acagaagaa tctgaagaaa ttgttacaag 540
 aagangtccc aaggtcacca aattcattga aggtgggtgat ggtctttat tgaagatgaa 600
 gaaattaaaa gacgcttcag ggaacnccc catgaaggaa ttgccagcca caaaaaatt 660
 cagggattag aaa 673

<210> 33
 <211> 673
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(673)
 <223> n = A,T,C or G

<400> 33
 actagtatt tactttcctc cgcttcagaa ggtttttcag actgagagcc taagcatact 60
 ggatctgttg ttcttttttg gtctcacctc atcagtgtgc atagtggcag aaattataaa 120
 gaagggtgaa aggagcaggg aaaagatcca gaagcatgtt agttcgacat catcatcttt 180
 tcttgaagta tgatgcatac tgcattattt tatttgcaaa ctaggaaattg cagtctgagg 240
 atcatttaga agggcaagtt caagaggata tgaagatttg agaacttttt aactattcat 300
 tgactaaaaa tgaacattaa tgttnaagac ttaagacttt aacctgctgg cagtcccaaa 360
 tgaattatg caactttgat atcatattcc ttgatttaaa ttgggctttt gtgattgant 420
 gaaactttat aaagcatatg gtcagttatt tnattaaaaa ggcaaaacct gaaccacctt 480
 ctgcacttaa agaagtctaa cagtacaaat acctatctat cttagatgga tntatttntt 540
 tntattttta aatattgtac tatttatggt nggtggggct ttcttactaa tacacaaatn 600
 aatttatcat ttcaanggca ttctatttgg gtttagaagt tgattccaag nantgcatat 660
 ttcgctactg tnt 673

<210> 34
 <211> 684
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(684)
 <223> n = A,T,C or G

<400> 34
 actagtatt tcaagaaaag aacttactga ttctctctgt cctaaagcaa gagtggcagg 60
 tgatcagggc tgggtgtagca tccggttcct ttagtgacgc taactgcatt tgtcactgat 120
 gaccaaggag gaaatcacta agacatttga gaagcagtgg tatgaacgtt cttggacaag 180
 ccacagtctc gagccttaac cctgtagttt gcacacaaga acgagctcca cctccccctc 240
 ttccaggagga atctgtgcgg atagattggc tggacttttc aatggttctg ggttgcaagt 300
 gggcactggt atggctgggt atggagcggg cagccccagg aatcagagcc tcagcccggc 360
 tgcctgggtg gaaggtaacag gtgttcagca ccttcggaaa aagggcataa agtngtgggg 420
 gacaattctc agtccaagaa gaatgcattg accattgctg gctatttgc tncctagtat 480
 gaattggatn catttttgac cangatnntt ctncatgct ttnttgcaat gaaatcaaat 540
 cccgcattat ctacaagtgg tatgaagtc tgcnncccc agagaggctg ttccaggcnat 600
 gtcttccaag ggcagggtgg gttacaccat ttacctccc ctctccccc agattatgna 660
 cncagaagga atttntttcc tccc 684

<210> 35
 <211> 614
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(614)
 <223> n = A,T,C or G

<400> 35
 actagtccaa cgcgttngcn aatattcccc tggtagccta ctctcttacc cccgaatat 60

```

ggtaagatcg agcaatggct tcaggacatg ggttctcttc tcctgtgac attcaagtgc 120
tcactgcatg aagactggct tgtctcagtg tntcaacctc accagggctg tctcttggtc 180
cacacctcgc tccctgttag tgcggtatga cagcccccat canatgacct tggccaagtc 240
acggtttctc tgtggccaat gttggtnggc tgattgggtg aaagtanggt ggaccaaagg 300
aagncncgtg agcagncanc nccagttctg caccagcagc gcctccgtcc tactnggggtg 360
ttcngtctc tcctggccct gngtgggcta nggctgatt cgggaanatg cctttgcang 420
gaagggganga taantgggat ctaccaattg attctggcaa aacnatntct aagattnttn 480
tgctttatgt ggganacana tctantctc atttnttgc gnanatnaca cctactcgt 540
gntcgancnc gtcttcgatt ttcgganaca cncantnaa tactggcggt ctgttgtaa 600
aaaaaaaaa aaaa 614

```

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<210> 36
<211> 686
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(686)
<223> n = A,T,C or G

```

```

<400> 36
gtggctggcc cggttctccg cttctcccca tccctactt tctccctcc ctcctcttcc 60
ctccctcgtc gactgttgct tgctggctgc agactccctg accctccct caccctccc 120
taacctcggg gccaccggat tgccctctct tccctgttgc ccagcccagc cctagtgtca 180
gggcgggggc ctggagcagc ccgaggcact gcagcagaag ananaaaaga cagcacnaac 240
ctcagctcgc cagtccggtc gctngcttcc gcgcgcattg caatnagaca gacgcgctc 300
acctgtctcg ggcacacgcg acccgtgggt gatttggcct tcagtggcat cacccttatg 360
ggtatttctt aatcagcgcg tgcaaagatg gttaacctat gctacgccag ggagatacag 420
gagactggat tggaaacatt ctggggctca aaggtctgtt tggggtgcaa cactgaataa 480
ggatgccacc aaagcagcta cagcagctgc agatttcaca gcccaagtgt gggatgctgt 540
ctcagganat naattgataa cctggctcat aacacattgt caagaattgt gatttcccca 600
ggatattatt atttgtttac cggggganag gataactgtt tcnctattt taattgaaca 660
aactnaaaca aaanctaagg aaatcc 686

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<210> 37
<211> 681
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(681)
<223> n = A,T,C or G

```

```

<400> 37
gagacanacn naacgtcang agaanaaaag angcatggaa cacaanccag gcncgatggc 60
cactttccca ccagcancca gcgccccca gngcccgang accangactc 120
cancctgnat caatctganc tctattcctg gccatncc acctcggagg tggangccgn 180
aaaggtcgca cnnncagaga agctgctgcc ancaccanc gccccnncc tgnccggctn 240
nataggaaac tggtgaccnn gctgcanaat tcatacagga gcacgcgag ggcaennnct 300
cacactgagt tnnngatgan gccnaccan ggacctncc cagcnnattg annacnggac 360
tgccgaggaa ggaagacccc gnacnggatc ctggccggcn tgccaccccc ccacccctag 420
gattcatncc cttgactgag tctctgaggg gctacccgaa cccgctccca tccctacca 480
natntgtctc natcgggact gacangctgg ggaatngagg ggctatcccc cancatcccc 540

```

```

tnanaccaac agcnacngan natnggggct cccnngggct ggngcaacnc tcctncaccc 600
cggcgcnnggc cttcggtgnt gtcctccttc aacnaattcc naaangggcg gccccccngt 660
ggactcctcn ttgttccttc c 681

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```

<210> 38
<211> 687
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(687)
<223> n = A,T,C or G

```

```

<400> 38
cnaaaaaaaa aaaacatggc cgaaaccagn aagctgcgcg atggcgccac ggccccctctt 60
ctccccggcct gtgtccggaa ggtttccctc cgaggcgccc cggctcccgc aagcggagga 120
gagggcgagg cgtgcggggg cggagctca nagggccctgg ggccgctctg ctctcccgcc 180
atcgcaaggg cggcgctaac cttagggctc cccgcaaagg tccccnange ggngggcgggc 240
gggggctgtg anaaccgcaa aaanaacgct gggcgcgcng cgaaccctgc ccccccgcg 300
aaggananaac ttccacagan gcagcgcttc cacagccan agccacnttc ctagggtgat 360
gcaccccgat aagttcctgn cggggaagct caccgctgtc aaaaaancctc ttgcgtccac 420
cggcgcacna agggggangan ggcannganc tgcgcgccgc acaggtcatc tgatcacgtc 480
gccccgccta ntctgctttt gtgaatcttc actttgttca accccacccg ccgttctctc 540
ctccttgctc cttctctctc ccttaanaac cagcttcttc taccnctatg tanttctctc 600
gcnchngtng aaattaattc ggtccnccgg aacctcttnc ctgtggcaac tgctnaaaga 660
aactgctgtc ctgnttactg cngtccc 687

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```

<210> 39
<211> 695
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(695)
<223> n = A,T,C or G

```

```

<400> 39
actagtctgg cctacaatag tgtgattcat gtaggacttc ttcatcaat tcaaaacccc 60
tagaaaaacg tatacagatt atataagtag ggataagatt tctaacattt ctgggctctc 120
tgacccctgc gctagactgt ggaaggggag tattattata gtatacaaca ctgctgttgc 180
cttattagtt ataacatgat aggtgctgaa ttgtgattca caatttaaaa acactgtaat 240
ccaaactttt ttttttaact gtagatcatg catgtgaatg ttaatgttaa ttgtttcaan 300
gttgcttatg gttagaaaaa ccacatgctt taaaatttta aaaagcaggg cccaaactta 360
ttagtttaaa attaggggta tgtttccagt ttgttattaa ntggttatag ctctgtttag 420
aanaaatcna ngaacangat ttngaaantc aagntgacat tatttnccag tgacttgta 480
atgtgaaatc anacacggca cttccgctt ttgtnctatc ggnntttgaa tccaanccg 540
ntccaaatct tnttggaaac ngtcctttta acttttttac nanatcttat tttttatttc 600
tggaatggcc ctatttaang ttaaaagggg ggggnnccac naccattctt gaataaaact 660
naatatatat ccttgggtccc ccaaatttta aggng 695

```

```

<210> 40
<211> 674
<212> DNA

```

```

<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(674)
<223> n = A,T,C or G

<400> 40
actagtagtc agttgggagt ggttgctata ccttgacttc atttatatga atttccactt      60
tattaaataa tagaaaagaa aatcccgggtg cttgcagtag agttatagga cattctatgc      120
ttacagaaaa tatagccatg attgaaatca aatagtaaag gctgttctgg ctttttatct      180
tcttagctca tcttaaataa gtagtacact tgggatgcag tgcgtctgaa gtgctaataa      240
gttgtaacaa tagcacaaat cgaacttagg atgtgtttct tctcttctgt gtttcgatct      300
tgatcaattc tttaatTTTg ggaacctata atacagtTTT cctattcttg gagataaaaa      360
ttaaatggat cactgatatt taagtcattc tgcttctcat ctnaatattc catattctgt      420
attagganaa antacctccc agcacagccc cctctcaaac cccacczaaa accaagcatt      480
tggaatgagt ctcttttatt tccgaantgt ggatgggata acccatatcn ctccaatTTT      540
tgnttggggt ggggtattaat ttgaactgtg catgaaaagn ggnaatctt nctttgggtc      600
aaanttttnc gggttaattg nctngncaaa tccaattctn ttttaagggtg tctttataaa      660
atttgcattt cngg                                     674

<210> 41
<211> 657
<212> DNA
<213> Homo sapien .

<220>
<221> misc_feature
<222> (1)...(657)
<223> n = A,T,C or G

<400> 41
gaaacatgca agraccacac actgtttgaa ttttgacaaa aaagtgactg tagggatcag      60
gtgatagccc cggaatgtac agtgtcttgg tgcaccaaga tgccttctaa aggctgacat      120
accttgggac cctaattggg cagagagtat agccctagcc cagtgggtgac atgaccactc      180
cctttgggag gctgaagtta aagggaatgg tatgtgtttt ctcatggaag cagcacatga      240
atnggttnaca ngatgttaaa ntaaggntct antttgggtg tcttgtcatt tgaaaaantg      300
acacactcct ancantggtt aaaggggtgc tgggaagccat ggaagaactc taaaaaacat      360
agcatgggct gatctgatta ctctctggca tcccgctcac ttttatggga agtcttatta      420
naaggatggg ananttttcc atatccttgc tgttggaaact ctggaacact ctctaaattc      480
ccctctatta aaaatcactg nccttactac acttctctct tganggaata gaaatggacc      540
tttctctgac ttagttcttg gcatggganc cagcccaaat taaaatctga ctnttccggt      600
ttctccngaa ctccactact tgaattggta aaacctcctt tgggaattagn aaaaacc      657

<210> 42
<211> 389
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(389)
<223> n = A,T,C or G

<400> 42

```



```

actagtgtctg aggaatgtaa acaagtttgc tgggccttgc gagacttcac caggttggtt      60
cgatagctca cactcctgca ctgtgcctgt caccagga tgtctttttt aattagaaga      120
caggaagaaa acaaaaacca gactgtgtcc cacaatcaga aacctccgtt gtggcagang      180
ggccttcacc gccaccaggg tgtcccgcca gacagggaga gactccagcc ttctgaggcc      240
atccgaaga attcctgttt ggggggttg gaggaaaaac acccggtatt aaaaagatgc      300
tggtgcctgc ccgcgtngtn ggggaaggac tgggttctctg gtgaatttct taaaagaaaa      360
atattttaag ttaagaaaaa aaaaaaaaaa

```

```

<210> 43
<211> 279
<212> DNA
<213> Homo sapien

```

```

<400> 43
actagtgcaca agtccttggc cttgagatgt cttctcgtta aggagatggg ccttttggag      60
gtaaaggata aaatgaatga gtctgtcat gattcactat tctagaacct gcattgacct      120
tactgtgtta gctctttgaa tgtctttgaa attttagact ttctttgtaa acaataata      180
tgtctttatc attgtataaa agctgttatg tgcaacagtg tggagatcct tgtctgattt      240
aataaaatac ttaaacactg aaaaaaaaaa aaaaaaaaaa

```

```

<210> 44
<211> 449
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(449)
<223> n = A,T,C or G

```

```

<400> 44
actagtagca tcttttctac aacgttaaaa ttgcagaagt agcttatcat taaaaaacia      60
caacaacaac aataacaata aatcctaagt gtaaatcagt tattctaccc cctaccaagg      120
atatacagct gttttttccc ttttttctcc tgggaataat tgtgggcttc ttcccaaat      180
tctacagcct ctttctctct ctcattgttg agcttccctg ttgtcacgca tgcgttgtgc      240
aagantgggc tgtttngctt ggantncggt ccnagtggaa ncattgcttc ccttggttac      300
gttggagaaa actcaaacct tcnancccta ggtgttncca ttttgtcaag tcatcactgc      360
atttttgtac tggcattaac aaaaaaagaa atnaaatatt gttccattaa actttaataa      420
aactttaaaa gggaaaaaaa aaaaaaaaaa

```

```

<210> 45
<211> 559
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(559)
<223> n = A,T,C or G

```

```

<400> 45
actagtgtgg gggaatcacg gacacttaaa gtcaatctgc gaaataattc tttttatcaca      60
cactcactga agtttttgag tcccagagag ccatctctat tcaaacattc caagtacttc      120
ttgagagccc agcattacat caacatgccc gtgcagttca aaccgaagtc cgcaggcaaa      180
tttgaagctt tgcttgtcat tcaaacagat gaaggcaaga gtattgctat tcgactaaat      240

```

```

ggcgaagctc ttggaaaaaa ttactagaa tacttttgt gttaagttaa ttacataagt 300
tgtattttgt taactttatc ttctacact acaattatgc ttttgtatat atattttgta 360
tgatggatat ctataattgt agattttgtt ttacaagct aatactgaag actcgactga 420
aatattatgt atctagccca tagtattgta cttaactttt acaggggtgaa aaaaaaatcc 480
tgtgtttgca ttgattatga tattctgaat aaatatggga atatatttta atgtgggtgaa 540
aaaaaaaaaa aaaaaggaa 559

```

```

<210> 46
<211> 731
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(731)
<223> n = A,T,C or G

```

```

<400> 46
actagttcta gtaccatggc tgcctatagat gcaaccatta tattccattt agttttctccc 60
tcaggttccc taacaattgt ttgaaactga atatatatgt ttatgtatgt gtgtgtgttt 120
actgtcatgt atatgggtga tatgggatgt gtgcagtttt cagttatata tataattcata 180
tatcacatatg catatatatg tataatatat atatatatat gcatacactt gtataatata 240
catatatata cacatatatg cacacatatn atcactgagt tccaaagtga gtcttttattt 300
ggggcaattg tattctctcc ctctgtctgc tcaactgggccc ttgcaagac atagcaattg 360
cttgattttc ttgggataag agtcttatct tccggcactct tgactctagc ctttaacttta 420
gattttctat ccagaatacc tctcatatct atcttaaaac ctaaganggg taaagangtc 480
ataagattgt agtatgaaag antttgctta gttaaaattat atctcaggaa actcatccat 540
ctacaaatta aattgtaaaa tgatgggtttg ttgratctga aaaaatgttt agaacaagaa 600
atgtaactgg gtacctgtta tatcaaagaa cctcnaattta ttaagtctcc tcatagcnaa 660
atccttatat ngcctctctc gacctgantt aatananact tgaataatga atagtttaatt 720
taggnttggg c 731

```

```

<210> 47
<211> 640
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(640)
<223> n = A,T,C or G

```

```

<400> 47
tgcgngccgg tttggccctt ctttgtanga cactttcatc cgccctgaaa tcttcccgat 60
cgttaataac tcctcaggtc cctgcctgca cagggttttt tcttantttg ttgcctaaca 120
gtacacccaaa tgtgacatcc ttccaccaat atngattnct tcataccaca tcntcnatgg 180
anacgactnc aacaattttt tgatnaccen aaanactggg ggctnnaana agtcantctt 240
ggagcagcat ggacctgtcn gcnactaang gaacaanagt nntgaacatt tacacaacct 300
ttggtatgtc ttactgaaag anagaaacat gcttctnncc cttagaccacg aggncaaccg 360
caganattgc caatgccaaag tccgagcggc tagatcaggt aatacatctc atggatgcac 420
tacatacnnt gtccccgaaa nanaagatgc cctaanggct tcttcnaact ggcccnгааа 480
acanctacac ctgggtgcttg ganaacanac tctttggaag atcatctggc acaagtctcc 540
cccagtgggg ttnccttgg cacctanctt accanactna ttccggaancc attctttgco 600
ntggccttnt ntgggacca ntcttctcac aactgnacc 640

```

<210> 48
 <211> 257
 <212> DNA
 <213> Homo sapien

<400> 48
 accagtatat gaaaatgtaa atatcacttg tgtactcaaa caaaagttgg tcttaagctt 60
 ccaccttgag cagccttgga aacctaacct gcctctttta gcataatcac attttctaaa 120
 tgattttctt tgttcctgaa aaagtgattt gtattagttt tacatttgtt ttttggaaga 180
 ttatatttgt atatgtatca tcataaaaata tttaaaataa aagtatcttt agagtgaaga 240
 aaaaaaaaaa aaaaaaa 257

<210> 49
 <211> 652
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (652)
 <223> n = A,T,C or G

<400> 49
 actagttcag atgagtggtt gctgaagggg ccccttcttc attttcatta taacccaatt 60
 tccacttatt tgaactctta agtcataaat gtataatgac ttatgaatta gcacagttaa 120
 gttgacacta gaaactgccc atttctgtat tacactatca aataggaaac attggaaga 180
 tggggaaaaa aatcttcttt taaaatggct tagaaaagtt tcagattact ttgaaaattc 240
 taaacttctt tctgtttcca aaacttgaaa atatgtagat ggactcatgc attaagactg 300
 ttttcaaagc tttcttcaca tttttaaagt gtgatttccc ttttaatata catatttatt 360
 ttcttttaaag cagctatata ccaacccatg accttggaga tatacctatn aaaccaatat 420
 aacagcangg ttattgaagc agctttctca aatgttgctt cagatgtgca agttgcaaat 480
 tttattgtat ttgtanaata caatttttgt tttaaactgt atttcaatct atttctcaa 540
 gatgcttttc atatagagtg aaatatccca ngataactgc ttctgtgtcg tgcatttga 600
 cgcataactg cacaaatgaa cagtgtatac ctcttggttg tgcattnacc cc 652

<210> 50
 <211> 650
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (650)
 <223> n = A,T,C or G

<400> 50
 ttgcgctttg atttttttag ggcttgtgcc ctgtttcact tatagggtct agaatgcttg 60
 tgrtgagtaa aaaggagatg cccaatatcc aaagctgcta aatgttctct ttgccataaa 120
 gactccgtgt aactgtgtga acacttggga ttttctctct ctgtcccagag gtctcgtct 180
 gctttctttt ttgggttctt tctagaagat tgagaaatgc atatgacagg ctgagancac 240
 ctccccaaac acacaagctc tcagccacan gcagcttctc cacagcccca gcttcgcaca 300
 ggctcctgga nggctgcctg ggggaggcag acatgggagt gccaaaggtg ccagatggtt 360
 ccaggactac aatgctctta tttttaactg ttgcccactg ctgccctcac ccttgcctgg 420
 ctctggagta cctgtgccc canacaagtg ggantgaaat ggggggtggg ggggaactg 480
 attcccantt agggggctgcc taactgaaca gtagggtatan aagggtgtgaa cctgngaant 540

gcttttataa attatnttcc ttgttanatt tatttttttaa ttttaactctt gctnaactgc 600
ccngggaaaaa ggggaaaaaaa aaaaaaaaat tctnttttaa cacatgaaca 650

<210> 51
<211> 545
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(545)
<223> n = A,T,C or G

<400> 51
tggcgtgcaa ccagggtagc tgaagtttgg gtctgggact ggagattggc cattaggcct 60
cctganattc cagctccctt ccaccaagcc cagctcttgc acgtggcaca gggcaaacct 120
gactcccttt gggcctcagt ttccccctcc ctccatgana tgaaaagaat actacttttt 130
cttgcttggtc taacnttgcg ggacncaaag tgnngtcatt attgctgtat tgggtgatgt 240
gtncaaaact gcagaagctc actgcctatg agaggaanta agagagatag tggatganag 300
ggacanaagg agtcattatt tggatatagat ccacccttcc caacctttct ctccctcagtc 360
cctgcncctc atgntcttgg tntggtagt cctttgtgcc accancctc atgcttttga 420
ttgtgtccat cctgggaagg ggtggnatcg tctcacaact tgttgcctc gtttganatg 480
catgctttct tnatnaaaca aanaaannaa tgtttgacag ngttttaaata aaaaaanaaa 540
caaaa 545

<210> 52
<211> 678
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(678)
<223> n = A,T,C or G

<400> 52
actagtagaa gaacttttgc gctttttgtgc ctctcacagg cgcctaaaagt cattgccatg 60
ggaggaagac gatttggggg gggagggggg gggggcangg tccgtggggc ttcccttant 120
ntatctccat ntccantggn cnntgtcgcc tcttccctcg tcnattinga anttantccc 180
tggnccecn nccctctccn nectnecct cccctctcgg ncnccctcnn cttttntan 240
ncttcccat ctcentccc cctnanngtc ccaacnccgn cagcaatnnc nacttntc 300
nctcncncc tccnccgctt cttctnttct cnactntntc ncnntnccn tgcnnntnaa 360
annctctccc cnetgcaanc gattctctcc ctccnncnn ctntccactc cntncttctc 420
nncgctcct ntntctnnc ccacctctc ccttcgnccc cantacnctc nccncccttn 480
cgnntcttn nnntcctcnn accnccncc tcccttence cctcttctcc cgggtntntc 540
tcttccnnc nncnncncc cncccttcc nngcgnccnt tccgccccn cncnccntt 600
ccttctcnc cantccaten cntntnccat nctnccncc nctcaccncc gctnccccn 660
ntctcttcca cactgtcc 678

<210> 53
<211> 502
<212> DNA
<213> Homo sapien

<220>

<221> misc_feature
 <222> (1)...(502)
 <223> n = A,T,C or G

<400> 53
 tgaagatcct ggtgtcgcca tgggcccgcg ccccgcccgt tggtaccggt attgtaagaa 60
 caagccgtac ccaaagtctc gcttctgccc aggtgtccct gatgccaaaa ttcgcatttt 120
 tgacctgggg cggaaaaang caaaantgga tgagtctccg ctttgtggcc acatgggtgtc 180
 agatcaatat gagcagctgt cctctgaagc cctgnangct gcccgaattt gtgccaataa 240
 gtacatggta aaaagtngtg gcnaagatgc ttccatatcc ggggtgcggnt ccaccccttc 300
 cacgtcatcc gcatcaacaa gatgttgtec tgtgtctggg ctgacaggct cccaacaggc 360
 atgcgaagtg cctttggaaa acccanggca ctgtggccag ggttcacatt gggccaattn 420
 atcatgttca tccgcaccaa ctgcagaaca angaacntgt naattnaagc cctgcccagg 480
 gncaanttca aatttcccgg cc 502

<210> 54
 <211> 494
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(494)
 <223> n = A,T,C or G

<400> 54
 actagtccaa gaaaaatatg cttaatgtat attacaaagg ctttgcataat gttaacctgt 60
 tttaatgccaa aaagtttgc tttgtccacaa tttccttaag acctcttcag aaagggattt 120
 gtttgcctta atgaatactg ttgggaaaaa acacagtata atgagtgaag agggcagaag 180
 caagaaattt ctacatctta gcgactccaa gaagaatgag tatccacatt tagatggcac 240
 attaatgagga ctttaattct tccttaaaaca caataatgtt ttcttttttc tttattccac 300
 atgttttcta agtatatttt tcatgcagga cagtttttca accttgatgt acagtgcactg 360
 tgctaaattt ttctttcagt ggcaacctct ataactttta aaatatgggt agcatcttgc 420
 ctgttttgaa ngggatatga chatnaatct atcagatggg aaatcctgtt tccaagttag 480
 aaaaaaaaaa aaaa 494

<210> 55
 <211> 606
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(606)
 <223> n = A,T,C or G

<400> 55
 actagtaaaa agcagcattg ccaaataatc cctaattttc cactaaaaat ataargaat 60
 gatgttaagc tttttgaaaa gtttaggtta aacctactgt tgtagatta atgtatttgt 120
 tgcttccctt tatctggaat gtggcattag cttttttact ttaacctctt ttaattctta 180
 ttcaattcca tgacttaagg ttggagagct aaacactggg atttttggat aacagactga 240
 cagttttgca taattataat cggcattgta catagaaaag acatggctac cttttgttaa 300
 atctgcactt tctaaatata aaaaaaggga aatgaagtat aaatcaattt ttgtataatc 360
 tgtttgaaac atgantttta tttgtctaat attanggctt tgcccttttc tgttagtctc 420
 ttgggatcct gtgtaaaact gttctcatta aacaccaaac agttaagctc attctctggt 480

```

actagctaca aattccgttt catattctac ntaacaattt aaattaactg aaatatctct 540
anatgggtcta cttctgtcnt ataaaaacna aacttgantt nccaaaaaaa aaaaaaaaaa 600
aaaaaa 606

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```

<210> 56
<211> 183
<212> DNA
<213> Homo sapien

```

```

<400> 56
actagtatat ttaaacttac aggcttatct gtaatgtaaa ccaccatttt aatgtactgc 60
aattaacatg gttataatac gtacaatcct tccctcatcc catcacacaa ctttttttgc 120
gtgtgataaa ctgatttttg tttgcaataa aaccttgaaa aataaaaaaa aaaaaaaaaa 180
aaa 183

```

```

<210> 57
<211> 622
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(622)
<223> n = A,T,C or G

```

```

<400> 57
actagtcact actgtcttct cttttagctt aatcaatcaa tattcttccc ttgcctgtgg 60
gcagtcggaga gtgctgtctg gtgtacgtg cacttgccca ctgagttggg gaagaggat 120
aatcagtgag cactgttctg ctgagagctc ctgattctacc ccacccctta ggatccagga 180
ctgggtcaaa gctgcatgaa accaggccct ggacgcaacc tgggaatggc tggagggtggg 240
agagaacctg acttctcttt cctctctccc cctccaacat tactggaact ctatctgttc 300
agggatcttc tgagcttgtt tccctgtctg gtgggacaga agacaaaagg gaagggangg 360
tctacaanaa gcagcccttc tttgtcctct ggggttaatg agcttgacct ananttcatt 420
gaganaccan aagcctctga tttttaattt ccttnaaatg tttgaagtnt atatntacat 480
atatataatt ctttnaatnt ttgagctctt gatattgtctt aaaatccant cctctctgcn 540
gaaacctgaa ttaaaacccat gaanaaaaat gtttncctta aagatgttan taattaattg 600
aaacttgaaa aaaaaaaaaa aa 622

```

```

<210> 58
<211> 433
<212> DNA
<213> Homo sapien

```

```

<400> 58
gaacaaattc tgattgggta tgtaccgtca aaagacttga agaaatttca tgattttgca 60
gtgtggaagc gttgaaaatt gaaagtact gcttttccac ttgctcatat agtaaaggga 120
tcctttcagc tgccagtgtt gaataatgta tcattccagag tgatgttata tgtgacagtc 180
accagcttta agctgaacca ttttatgaat accaaaataa tagacctctt gtactgaaaa 240
catatttggt actttaatcg tgctgcttgg acagaaatat ttttactggc tcttctgaat 300
tgacagttaa cctgtccatt atgaatggcc tactgtctta ttatttgttt tgacttgaat 360
ttatccacca aagacttcat ttgtgtatca tcaataaagt tgtatgtctc aactgaaaaa 420
aaaaaaaaa aaa 433

```

```

<210> 59
<211> 649

```

```

<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(649)
<223> n = A,T,C or G

<400> 59
accagttcatt atctgacttt cngggtataa tcattctaata gagtgtgaag tagcctctgg      60
tgtcatttgg atttgcattt ctctgacgag tgatgctatc aagcaccttt gctgggtgctg      120
ttggccatat gtgratgttc cctggagaag tgtctgtgct gagccttggc ccacttttta      180
attagggcgtt tgtcttttta ttactgagtt gtaaganttc tttatatatt ctggattcra      240
gacccttata agatacatgg ttgtcaaata tttctccca ttctgtgggt tgtgctttca      300
ctttatcgat aatgtcctta gacatataat aaatttgtat tttaaaagtg acttgatttg      360
ggctgtgcaa ggtgggctca cgcttgtaat cccagcactt tgggagactg aggtgggtgg      420
atcatatgan gangctagga gttcgaggtc agcctggcca gcatagcgaa aacttgcctc      480
tacnaaaaaa acaaaaatta gtcaggcatg gtggtgcacg tctgtaatac cagcttctca      540
ggangctgan gcacaaggat cacttgaacc ccagaangaa gangttgcag tgancagaag      600
atcatgccag ggcaacaaaa atgagaactt gtttaaaaaa aaaaaaaaaa      649

<210> 60
<211> 423
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(423)
<223> n = A,T,C or G

<400> 60
actagttcag gccttccagt tcactgacaa acatggggaa gtgtgcccag ctggctggaa      60
acctggcagt gataccatca agcctgatgt ccaaaagagc aaagaatatt tctccaagca      120
gaagtgaagc ctgggctggt ttagtgccag gctgcgggtg gcagccatga gaacaaaacc      180
tcttctgtat tttttttttc cattagtana acacaagact cngattcagc cgaattgtgg      240
tgtcttacaa ggcagggtct tcctacaggg ggtgganaaa acagcctttc ttcccttggt      300
aggaatggcc tgagttggcg ttgtgggcag gctactggct tgtatgatgt attagtagag      360
caaccattta atcttttcta gtttcatna aacttganct gagaccttaa acaaaaaaaa      420
aaa
423

<210> 61
<211> 423
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(423)
<223> n = A,T,C or G

<400> 61
cgggactgga atgtaaagtg aagttcggag ctctgagcac gggctcttcc cgccgggtcc      60
tccctcccca gacccagag ggagaggccc accccgcca gccccgccc agccctgct      120
caggctctgag tatggctggg agtcgggggc cacaggcctc tagctgtgct gctcaagaag      180

```

```

actggatcag ggtanctaca agtggccggg ccttgccttt gggattctac cctgttccta 240
atttggtgtt ggggtgcggg gtccctggcc cccttttcca cactnccctc cccngacag 300
caacctccct tggggcaatt gggcctggnt ctcncccgnt tggtgcnacc ctttgttgg 360
ttaaggncct taaaaatgtt annttttccc ntgcctgggt taaaaaagga aaaaactnaa 420
aaa 423

```

```

<210> 62
<211> 683
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(683)
<223> n = A,T,C or G

```

```

<400> 62
gctggagagg ggtacggact ttcttggagt tgtcccaggt tggaaatgaga ctgaactcaa 60
gaagagaccc taagagactg ggaatgggt cctgccttca ggaaagtga agacgcttag 120
gctgtcaaca cttaaaaggaa gtcccttga agcccagagt ggacagacta gaccattga 180
tggggccact ggccatggtc cgtggacaag acattccngt gggccatggc acaccggggg 240
ggatcaaaaat gtgtacttgt ggggtctcgc cccttgccaa aaccaaacca ntccactcc 300
tgtcttggga ctttcttccc attccctccc ccccaaatgc acttcccttc cctcctctgc 360
ccctcctgtg tttttggaat tctgtttccc tcaaaattgt taatttttta ntcttngacc 420
atgaacttat gtttggggtc nangttcccc ttnccaatgc atactaatat attaatgggt 480
atttattttt gaaatatttt ttaatgaact tggaaaaaat tnnatggaat tccctncttc 540
catttttttt ggggggggtg gggggntggg ttaaaatttt ttgggaancc snatnggaaa 600
ttnttacttg gggcccccct naaaaaantn anttccaact ctttnnatngc cctnttccn 660
ctaaaaaaa ananannaaa aan 683

```

```

<210> 63
<211> 731
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(731)
<223> n = A,T,C or G

```

```

<400> 63
actagtcata aagggtgtgc gcgtcttcga cgtggcggtc ttggcgccac tgctgcgaga 60
cccggccctg gacctcaagg tcatccactt ggtgcgtgat ccccgcgagg tggcgagttc 120
acggatccgc tcgcgccacg gcctcatccg tgagagccta cagggtggtg gcagccgaga 180
ccgcgagctc accgcatgcc cttcttggag gccgcggggc acaagcttgg cgcccanaaa 240
gaaggcgtng ggggcccga aantaccacg ctctggcgcc tatggaangt cctcttgcaa 300
taatatgtgt tnaaaanctg canaanagcc cctgcancce cctgaactgg gntgcagggc 360
cncttacctn gtttggntgc ggttaciaag aacctgtttn ggaaaacctt nccnaaaacc 420
ttccgggaaa atttntcaaa ttttnttgg ggaattnttg ggtaaaacct ccnaaaatgg 480
gaaacntttt tgccctnnaa antaaacct tnggttccgg gggccccccc ncaaaaacct 540
ttttntttt tctntgcccc cantnncccc ccggggcccc ttttttntng ggaaaanccc 600
ccccctncc nanantttta aaaggngggg anaatttttn nttncccccc gggncccccn 660
ggngntaaaa nggtttcncc ccccagagg gnggggnhnc ctcnnaaacc cntntcnna 720
cncntcttn n 731

```


<210> 64
 <211> 313
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(313)
 <223> n = A,T,C or G

<400> 64
 actagttgtg caaaccacga ctgaagaaag acgaaaagtg ggaaataact tgcaacgtct 60
 gtagagatg gttgctacac atgttgggtc ttagagagaaa catcttgagg agcagattgc 120
 taaagttgat agagaatatg aagaatgcat gtcagaagat ctctcggaaa atattaaaga 180
 gattagagat aagtatgaga agaaagctac tctaattaag tcttctgaag aatgaagatn 240
 aaatgttgat catgtatata tatccatagt gaataaaatc gtctcagtaa agttgraaaa 300
 aaaaaaaaaa aaa 313

<210> 65
 <211> 420
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(420)
 <223> n = A,T,C or G

<400> 65
 actagttccc tggcaggcaa gggcttccaa ctgaggcagt gcatgtgtgg cagagagagg 60
 caggaaagctg gcagtggcag ctctgtgttc tagggagggg tgtggctccc tcttccctg 120
 tctgggaggt tggagggaag aatctaggcc ttagcttgcc ctctgccac ccttccctt 180
 gtagatactg ccttaacact ccctcctctc tcagctgtgg ctgccacca agccagggtt 240
 cctcgtgctc actaatttat ttccaggaaa ggtgtgtgga agacatgagc cgtgrataat 300
 atttgtttta acattttcat tgcaagtatt gaccattatc ctgtgtgtg tatcgttga 360
 acacaaatta atgatattaa aaagcatcca aacaaagccn annnnnaana nnannngaaa 420

<210> 66
 <211> 676
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(676)
 <223> n = A,T,C or G

<400> 66
 actagtttcc tatgatcatt aaactcatcc tcagggttaa gaaaggaatg taaatttctg 60
 cctcaatttg tacttcatca ataagttttt gaagagtgcg gatttttagt caggtcttaa 120
 aaataaaact acaaatctgg atgcatttct aaattctgca aatgtttcct ggggtgactt 180
 aacaaggaat aatccacaa tatacctagc tacctaatac atggagctgg ggctsaacct 240
 actgttttta aggatttgct ctacttctg gctgaggaaa aataagtagt tccgagggaa 300
 gtagttttta aatgtgagct tatagatngg aaacagaata tcaacttaat tatggaaatt 360
 gtagaacc tgtctctctg ttatctgaat ctgattgca attactattg tactggatag 420

```

actccagccc attgcaaagt ctcagatata ttanctgtgt agttgaatc cttggaaatt 480
ctttttaaga aaaaattgga gtttnaaaga aataaacccc tttgttaaat gaagcttggc 540
tttttgggtga aaaanaatca tcccgcaggg cttattgttt aaaaanggaa ttttaagcct 600
ccctggaaaa anttgtaaat taaatgggga aaatgntggg naaaaattat ccgttagggc 660
ttaaagggaa aactta                                     676

```

```

<210> 67
<211> 620
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(620)
<223> n = A,T,C or G

```

```

<400> 67
caccattaaa gctgcttacc aagaacctcc ccagcatttt gacttccttg tttgatagct 60
gaattgtgag caggtgatag aagagccctt ctagtgaac atacagataa tttgctgaat 120
acattccatt taatgaaggg gttacatctg tcacgaagct actaagaagg agcaagagca 180
taggggaaaa aaatctgata agaacgcata aaactcacat gtgccccctc tactacaaa 240
agattgtagt gctgtggtgg tttattccgt tgtgcagaa ttgcaagctg agtcactaaa 300
cccaaagaga ggaaattata ggtagttaa acattgtaat cccaggaact aagttaatt 360
cacttttgaa gtgttttctt ttttattttt ggttgtctg atttactttg ggggaaaang 420
ctaaaaaaa agggatatca atctctaatt cagtgtccac taaaagtgt ccctaaaaag 480
tctttactgg aanttatggg actttttaag ctcaggntt tttggtctc caaattaacc 540
ttgcatgggc ccttataaat tgttgaangg cattctctgc tctaagtttg gggaaaattc 600
ccccnctttn aaaatttga                                     620

```

```

<210> 68
<211> 551
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(551)
<223> n = A,T,C or G

```

```

<400> 68
actagtagct ggtacataat cactgaggag ctatttctta acatgctttt atagaccatg 60
ctaattgctag accagtatct aagggttaat ctcacacctc cttagctgta agagtctggc 120
ttagaacaga cctctctgtg caataacttg tggccactgg aaatccctgg gccggcattt 180
gtattggggg tgcaatgact cccaagggcc aaaagagtta aaggcacgac tgggatttct 240
tctgagactg tggtgaaact ccttccaagg ctgagggggg cagtangtgc tctgggaggg 300
actcggcacc actttgatat tcaacaagcc acttgaagcc caattataaa attgttattt 360
tacagctgat ggaactcaat ttgaaccttc aaaactttgt tagtttatcc tattatattg 420
ttaaacctaa ttacatttgt ctagcattgg atttgggtcc tgtngcatat gttttttctn 480
cctatgtgct cccctcccc nnatcttaat ttaaacnca attttgcnat tcnccnnnnn 540
nannnnanna a                                     551

```

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<210> 69
<211> 396
<212> DNA
<213> Homo sapien

```

<220>
<221> misc_feature
<222> (1)...(396)
<223> n = A,T,C or G

<400> 69
cagaaatgga aagcagagtt ttcatttctg tttataaacg tctccaaaca aaaatggaaa 60
gcagagtttt cattaaatcc ttttaccttt tttttttctt ggtaatcccc tcaaataaca 120
gtatgtggga tattgaatgt taaagggata tttttttcta ttatttttat aattgtacaa 180
aattaagcaa atgttaaaag ttttataatg tttattaatg ttttcaaaag gtatnataca 240
tgtgatacat tttttaagct tcagttgctt gtcttctggt actttctgtt atgggctttt 300
ggggagccan aaaccaatct acnatctctt tttgtttgcc aggacatgca ataaaaatta 360
aaaaataaat aaaaactatt nagaaattga aaaaaa 396

<210> 70
<211> 536
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(536)
<223> n = A,T,C or G

<400> 70
actagtgcga aagcaaatat aaacatcgaa aaggcgttcc tcacgttagc tgaagatata 60
cttcgaaaaga cccctgtaaa agagcccaac agtgaaaatg cagatatacag cagtggagga 120
ggcgtgacag gctggaagag caaatgctgc tgagcattct cctgttccat cagttgccat 180
ccactacccc gttttctctt cttgctgcaa aataaaccac tctgtccatt ttaactcta 240
aacagatatt tttgtttctc atcttaacta tccaagccac ctattttatt tgttcttca 300
tctgtgactg cttgctgact ttatcataat tttcttcaaa caaaaaaatg tatagaaaaa 360
tcattgtcgt gacttcattt ttaaagtnta cttgctcagc tcaactgcat ttcagttgtt 420
ttatagtcca gttcttatac acattnaaac ccatngcaat catttcaaat ctattctgca 480
aattgrataa gaataaaaagt tagaatttaa caattaaaaa aaaaaaaaaa aaaaaa 536

<210> 71
<211> 865
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(865)
<223> n = A,T,C or G

<400> 71
gacaaagcgt taggagaaga anagaggcag ggaanactnc ccaggcacga tggccnccct 60
cccaccagca accagcgcgc cccaccagcc cccaggcccg gacgacgaag actccatcct 120
ggattaatct nacctctntc gcctgnccca ttctacctc ggaggtggag gccggaaagg 180
tcncaccaag aganaantcgt ctgccaacac caaccgccc agccctggcg ggcacganag 240
gaaactggtg accaatctgc agaattctna gaggaanaag cnaggggccc cgcgctnaga 300
cagagctgga tatgangcca gaccatggac nctacnccn ncaatncana cgggactgag 360
gaagatggan gaccnccgac nngatcaggc cngctnncca nccccccacc cctatgaatt 420
attcccgctg aangaattct tgannngctt ccannaaagc gcctccccnc cnaacgnaan 480

```

tncaacatng ggattanang ctgggaactg naaggggcaa ancctnnaat atccccagaa 540
acaanctctc ccnaanaaac tggggcncct catnggtggn accaaactatt aactaaaccg 600
cacgccaagn aantataaaa ggggggcccc tccncggngg accccctttt gtcccttaat 660
ganggttatc cnccttgctg accatggtnc ccnnttctgt ntgnatgttt ccnctcccc 720
ccncttatnt cnagccgaac tennatttnc cggggggtgc nactnantng tncnctctn 780
ttngttgncc cngccctttc cngcggaaacn cgtttccccc ttantaacgg caccgggggn 840
aagggtgntt ggccccctcc ctc 865

```

```

<210> 72
<211> 560
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(560)
<223> n = A,T,C or G

```

```

<400> 72
cctggacttg tcttggttcc agaacctgac gaccggcgga cggcgacgtc tcttttgact 60
aaaagacagt gtccagtgtc ccngcctagg agtctacggg gaccgcctcc cgcgcgcga 120
ccatgcccaa cttctctggc aactggaaaa tcatccgata ggaaaacttc gangaattgc 180
tonaantgct ggggggtgaat gtgatgctna ngaanattgc tgtggctgca gcgtccaagc 240
cagcagtgga gatcnaacag gagggagaca ctttctacat caaaacctcc accaccgtgc 300
gcaccacaaa gattaaactc nnngttgggg agganattga ggancaaaact gtggatngga 360
ngcctgtnaa aacttggtga aatgggagaa tganaataaa atggtctgtg ancaaaaact 420
cctgaaggga gaaggccccc anaactcctg gaccngaaaa actgaccenc cnatngggga 480
actgatnctt gaacctgaa cgggggggat ganccttttt tnttgcencc naanggggtc 540
tttcnctttc ccaaaaaaaa 560

```

```

<210> 73
<211> 379
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(379)
<223> n = A,T,C or G

```

```

<400> 73
ctggggganc ggcggtngc nccatntcnn gncgcgaagg tggcaataaa anccnctga 60
aaccgcncaa naaacatgcc naagatatgg acgaggaaga tngngctttc nngnacaaac 120
gnannagga acanaacaaa ctcnangagc tctcaagcta atgcccgggg gaaggggccc 180
ttggccacnn gtggaattaa gaaatctggc aaanngtann tgttcttctg gcctnangag 240
ataagngacc ctttatttca tctgtattta aacctctctn tccctgnca taacttcttc 300
tncacgtan agntggaant anttgttctc ttggactgtt gtncaattta gannaaactc 360
ttgttcaaaa aaaaaataa 379

```

```

<210> 74
<211> 437
<212> DNA
<213> Homo sapien

<220>

```

<221> misc_feature
 <222> (1)...(437)
 <223> n = A,T,C or G

<400> 74
 actagttcag actgccacgc caaccccaga aaatacccca catgccagaa aagtgaagtc 60
 ctagggtgtt ccatttatgt ttcaatctgt ccatttacca ggcctcgcga taaaaacaaa 120
 acaaaaaaac gctgccaggt ttanaagca gttctggtct caaaaccatc aggatcctgc 180
 caccaggggt cttttgaaat agtaccacat gtaaaaggga atttggtctt cacttcattc 240
 aatcactgaa ttgtcaggct ttgattgata attgtagaaa taagtagcct tctgtgtgtg 300
 gaataagtta taatcagtat tcatctcttt gttttttgtc actcttttct ctctnattgt 360
 gtcatttgta ctgtttgaaa aatatttctt ctataaaatt aaactaacct gccttaaaaa 420
 aaaaaaaaaa aaaaaaa 437

<210> 75
 <211> 579
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(579)
 <223> n = A,T,C or G

<400> 75
 ctccgtcgcg gccaaagatga tgtgcggggc gccctccgcc acgcagcagg ccaccgcga 60
 gaccagcac atccgccgacc aggtgagggt ccagcttgaa gagaaagaaa acaagaagtt 120
 cctgtgtgtt aaggccgtgt cattcaagag ccagggtgtc gcggggacaa actacttcat 180
 caagggtcac gtcggcgacg aggtacttct acacctgcga gtgttccaat ctctccctca 240
 tgaaaacaag cctttgacct tatctaacta ccagaccaac aaagccaagc atgatgagct 300
 gacctatttc tgatccgtac ttggacaag gcccttcagc cagaagactg acaaaagctat 360
 cctccgtcta ccagagcgtg cacttgtgat cctaaaataa gcttcattct cgggctgtgc 420
 ccttgggggt gaaggggcan gatctgcact gcttttgcatt ttctcttctt aaatttcatc 480
 gtgttgattc tttccctcca ataggtgatc ttnattactt tcagaatatt ttccaaatna 540
 gatatatatt naaaatcctt aaaaaaaaaa aaaaaaaaaa 579

<210> 76
 <211> 666
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(666)
 <223> n = A,T,C or G

<400> 76
 gtttatccta tcttcccaac cagattgtca gctccttgag ggcaagagcc acagtatatt 60
 tccccgtttc ttccacagtg cctaataata ctgtggaact aggttttaaat aattttttaa 120
 ttgatgttgt tatgggcagg atggcaacca gaccattgtc tcagagcagg tgctggctct 180
 ttccctggcta ctccatgttg gctagcctct ggtaacctct tacttattat cttcaggaca 240
 ctactacag ggaccaggga tgatgcaaca tccctgtctt ttatgacag gatgtttgct 300
 cagcttctcc aacaataaaa agcagctggt aaaaacttg cggaattctt ggactgtttt 360
 caaaaaatat acagtttacc gaaaatcata ttatcttaca atgaaaagga ntttatagat 420
 cagccagtga acaacctttt ccaccatac aaaaattctt tttccgaan gaaaanggct 480

```

ttctcaataa nccctcacttt cttaanatct tacaagatag ccccganatt ttatcgaaac 540
tcatttttagg caaatatgan tttttattgtt cgttacttgt ttcaaaattt ggtattgtga 600
atatcaatta ccaccccat ctcccatgaa anaaanggga aanggtgaan ttcntaancg 660
cttaaa 666

```

```

<210> 77
<211> 396
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(396)
<223> n = A,T,C or G

```

```

<400> 77
ctgcagcccg ggggatccac taatctacca nggttatttg gcagctaatt ctanatttgg 60
atcattgccc aaagttgcac ttgctggtct cttgggattt ggccttgga aggtatcata 120
catanganta tgccanaata aattccattt ttttgaaaat canctccntg gggctggttt 180
tggccacacag cataacangc actgcctcct tacctgtgag gaatgcaaaa taaagcatgg 240
attaagttag aaggagagact ctgagccttc agcttcctaa attctgtgtc tgtgactttc 300
gaagtttttt aaacctctga attgttacac atttaaaatt tcaagtgcac tttaaaataa 360
aatacttcta atgggaacaa aaaaaaaaaa aaaaaa 396

```

```

<210> 78
<211> 793
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(793)
<223> n = A,T,C or G

```

```

<400> 78
gcattcctagc cgcgactca cacaaggcag gtgggtgagg aaatccagag ttgccatgga 60
gaaaattcca gtgtcagcat tcttgctcct tgtggccctc tcttacactc tggccagaga 120
taccacagtc aaacctggag ccaaaaagga cacaaggac tctcgacca aactgccccca 180
gacctcttcc agaggttggg gtgaccaact catctggact cagacatatg aagaagctct 240
atataaatcc aagacaagca acaaaccttt gatgattatt catcacttgg atgagtgcc 300
acacagtcna gctttaaaga aagtgtttgc tgaaaataaa gaaatccaga aattggcaga 360
gcagtttgtc ctctcaatc tggtttatga aacaactgac aaacaccttt ctctgatgg 420
ccagtatgtc ccaggattat gtttgttgac ccattctctga cagttgaagc cgatatcctg 480
ggaagatatt cnaaccgtct ctatgcttac aaactgcaga tacgctctgt tgcttgacac 540
atgaaaaagc tctcaagttg ctnaaatga attgtaagaa aaaaaatctc cagcctcttg 600
tctgtcggct tgaaaattga aaccagaaaa atgtgaaaaa tggctattgt ggaacanatn 660
gacacctgat taggttttgg ttatgttcac cactattttt aanaaaanan ntcttaaaat 720
ttgggtcaat tntctttttn aaacaatntg tttctacntt gngancatgat ttctaaaaaa 780
aataatnttt ggc 793

```

```

<210> 79
<211> 456
<212> DNA
<213> Homo sapien

```

<220>
 <221> misc_feature
 <222> (1)...(456)
 <223> n = A,T,C or G

<400> 79

actagtatgg ggtgggaggc cccacccttc tcccctaggc gctgttcttg ctccaaaggg	60
ctccgtggag agggactggc agagctgang ccacctgggg ctggggatcc cactcttctt	120
gcagctgttg agcgcaccta accactgggc atgccccac cctgtctctc cgcaccgcct	180
tcctcccgac cccangacca ggctacttct cccctcctct tgcctccctc ctgccccgc	240
tgcctctgat cgtangaatt gangantgtc ccgccttggt gctganaatg gacagtggca	300
ggggctggaa atgggtgtgt gtgtgtgtgt gtgtgtgtgt gtgtgtgtgt gcnccccccc	360
tgcaagaccg agattgaggg aaancatgtc tgcctgggtgt gaccatgttt cctctccata	420
aanctccccct gtgacnctca naaaaaaaaa aaaaaa	456

<210> 80
 <211> 284
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(284)
 <223> n = A,T,C or G

<400> 80

ctttgtacct ctgaaaaaga taggtattgt gtcattgaaac ttgagtttaa attttatata	60
taaaactaaa agtaatgctc accttagcaa cacatactaa aattggaacc atactgagaa	120
gaatagcatg accccgtgc aaacaggaca agcaaatttg tgatgtgttg attaaaaaga	180
aataaataaa tgtgtatatg tgtaacttgt atgtttatgt ggaatacaga ttgggaaaaa	240
aaatgtattt cttactgtga aaaaaaaaaa aaaaaaaaaa aana	284

<210> 81
 <211> 571
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(571)
 <223> n = A,T,C or G

<400> 81

gccaccaaca ttccaagcta ccctgggtac ctttgtgcag tagaagctag tgagcatgtg	60
agcaagcggc gtgcacacgg agactcatcg ttataattta ctatctgcc aagtagaaaa	120
gaaaggctgg ggatatttgg gttggcttgg ttttgatttt ttgcttggtt gtttgttttg	180
tactaaaaca gtattatctt ttgaatatcg tagggacata agtatataca tgttatccaa	240
tcaagatggc tagaatgggt cctttctgag tgtctaaaac ttgacacccc tggtaaatct	300
ttcaacacac ttttactgcc tgcgtaatga agttttgatt catttttaac cactggaaat	360
tttcaatgcc gtcatcttca gttagatnat ttgacacttt gagattaaaa tggcatgtct	420
atttgattag tcttattttt ttatttttac aggcctatca gtctcactgt tggctgtcat	480
tgtgacaaaag tcaataaaac ccccnaggac aacacacagt atgggatcac atattgtttg	540
acattaagct ttggccaaaa aatgttgcac gtgttttacc tgcacttgct aaatcaatan	600
caaaaaggct ggctnataat gttgtgtgtg aaataattca tnancaacca aaaaaaaaaa	660
aaaaaaaaa a	671

<210> 82
 <211> 217
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(217)
 <223> n = A,T,C or G

<400> 82
 ctgcagatgt tctctgaatg ctttgtcaaa ttaanaaaagt taaagtgcaa taatgtttga 60
 agacaataag tgggtggtgta tcttgtttct aataagataa acttttttgt ctttgcttta 120
 tcttcattagg gagttgtatg tcagtgtata aaacatactg tgtggtataa caggcttaat 180
 aaattcttta aaaggaaaaa aaaaaaaaaa aaaaaaa 217

<210> 83
 <211> 460
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(460)
 <223> n = A,T,C or G

<400> 83
 cgcgagtggg agcaccagga tctcgggctc ggaacgagac tgcacggatt gttttaagaa 60
 aatggcagac aaaccagaca tgggggaaat cgccagcttc gatnaggcca agctgaanaa 120
 aacggagacg caggagaaga acaccctgcc gaccaaagag accattgagc angagaagcg 180
 gagtgaattt tcttaagatc ctggaggatt tcttaccctc gtcctcttcg agacccagc 240
 cgtgatgtgg aggaagagcc acctgcaaga tggacacgag ccacaagctg cactgtgaac 300
 ctgggcactc cgcgcgatg ccaccggcct gtgggtctct gaagggaccc cccccaatcg 360
 gactgccaaa ttctccggtt tgcccggga tattatacaa nattatttct atgaataatg 420
 annataaaac acacctcgtg gcancaana aaaaaaaaaa 460

<210> 84
 <211> 323
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(323)
 <223> n = A,T,C or G

<400> 84
 tgggtgatct tggctctgtg gagctgctgg gacgggatct aaaagactat tctggaagct 60
 gtggtccaan gcattttgct ggcttaacgg gtcccggaac aaaggacac agctctctaa 120
 aattgaagtt taccganat aacaatcttt tgggcagaga tgcctatttt aacaaacncc 180
 gtccctgcgc aacaacnaac aatctctggg aaataccggc catgaacntg ctgtctcaat 240
 cnancatctc tctagctgac cgatcatatc gtcccagatt actacanatc ataataattg 300
 atttctctga naaaaaaaaa aaa 323

<210> 85
<211> 771
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(771)
<223> n = A,T,C or G

<400> 85
aaactgggta ctcaacactg agcagatctg ttctttgagc taaaaacat gtgctgtacc 60
aanagtttgc tcctggctgc tttgatgtca gtgctgtac tccacctctg cggcgaatca 120
gaagcaagca actttgactg ctgtcttgga tacacagacc gtattcttca tccraaattt 180
attgtgggct tcacacggca gctggccaat gaaggctgtg acatcaatgc tatcatcttt 240
cacacaaaga aaaagttgtc tgtgtgcgca aatccaaaac agacttgggt gaaatatatt 300
gtgcgtctcc tcagtataaa agtcaagaac atgtataaac tgtggctttt ctggaatgga 360
attggacata gcccagaac agaaagaact tgcctgggtt ggaggtttca ctgcacatc 420
atgganggtt tagtgcttat cttatttgtg cctcctggac ttgtccaatt natgaagtta 480
atcatattgc atcatanttt gctttgttta acatcacatt naaattaaac tgtattttat 540
gttatttata gctntaggtt ttctgtgttt aactttttat acnaantttc ctaaactatc 600
ttgggtntant gcaanttaaa aatttatatt ggggggggaa taaatattgg antttctgca 660
gccacaagct ttttttaaaa aaccantaca nccnngttaa atggtnggtc cnaatgggt 720
tttgcctttt antagaaaaa ttnttagaac natttgaaaa aaaaaaaaaa a 771

<210> 86
<211> 628
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(628)
<223> n = A,T,C or G

<400> 86
actagtttgc tttacatttt tgaaaagtat tttttttgtc caagtgttta tcaactaaac 60
cttgtgttag gtaagaatgg aatttattaa gtgaatcagt gtgaccttc ttgtcataag 120
attatcttaa agctgaagcc aaaatatgct tcaaaagaaa angactttat tgttcattgt 180
agttcatata ttcaaagcat ctgaactgta gtttctatag caagccaatt acatccataa 240
gtggagaang aaatagatta atgtcnaagt atgattggtg gagggagcaa ggttgaagat 300
aatctggggt tgaaattttt tagttttcat tctgtacatc tttagttnga catcagattt 360
gaaatattaa tgtttacctt tcaatgtgtg gtatcagctg gactcantaa cacccttttc 420
ttccctnngg gatggggaat ggattattgg aaaatggaaa gaaaaaagta cttaaagcct 480
tcctttcnca gtttctggct cctaccctac tgatttancc agaataagaa aacattttat 540
catcntctgc tttattccca ttaatnaant tttgatgaat aaatctgctt ttatgcnnac 600
ccaaggaatt nagtggnttc ntctttgt 628

<210> 87
<211> 518
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature

<222> (1)...(518)

<223> n = A,T,C or G

<400> 87

ttttttat	tttttagaga	gtagttcagc	ttttatttat	aaattttattg	cctgttttat	60
tataacaaca	ttatactggt	tatggtttaa	tacatatggg	tcaaaatgta	taatacatca	120
agtagtacag	ttttaaaatt	ttatgcttaa	aacaagtttt	gtgtaaaaaa	tcgagataca	180
ttttacatgg	caaatcaatt	tttaagtcac	cctaaaaatt	gatttttttt	tgaaatttaa	240
aaacacattt	aatttcaatt	tctctcttat	ataaccttta	ttactatagc	atggttttca	300
ctacagttaa	acaatgcagc	aaaattccca	tttcacggta	aattgggttt	taagcggcaa	360
ggttaaaatg	ctttgaggat	cctnaatacc	ctttgaactt	caaatgaagg	ttatggctgt	420
naatttaacc	ctcatgccat	aagcagaagc	acaagtttag	ctgcattttg	ctctaaactg	480
taaaancgag	ccccccggtg	aaaaagcaaa	agggaccc			518

<210> 88

<211> 1844

<212> DNA

<213> Homo sapien

<400> 88

gagacagcga	atcttagtat	caaaggattt	ttggcctcag	aaaaagttgt	tgattatctt	60
tattttat	tattttcga	gactccgtct	caaaaaaaaa	aaaaaaaaaa	agaatcacia	120
ggtatttgc	aaagcatttt	gagctgcttg	gaaaaaggga	agtagttgca	gtagagtttc	180
ttccatcttc	ttgggtgctg	gaagccatat	atgtgtcttt	tactcaagct	aagggtgata	240
agcttatgtg	ttgaatttgc	tacatctata	ttccacatat	tctcacataa	agagaattct	300
gaaatagaaa	tatcatagaa	catttaagaa	agtttagtat	aaataatatt	ttgtgtgtct	360
taattccctt	gaagggatct	atccaaagaa	aattattttac	actgagctcc	ttcctacacg	420
ttccagtaac	agatcctgtg	ttagtctttg	aaaatagctc	attttttaaa	tgctcagtag	480
tagatgtagc	atcacataga	tgtataatga	cgtgtattat	gttaacaatg	tctgcagact	540
ttgtaggaat	acaaaacatg	gccttttttt	taagcaaaac	gggccaatga	ctagaataac	600
acataaggga	atctgtgaat	atgtattata	agcagcattc	cagaaaaagta	gttgggtgaa	660
taattttcaa	gtcaaaaagg	gatatggaaa	gggaattatg	agtaacctct	attttttaag	720
ccttgctttt	aaattaaacg	ctacagccat	ctaaagcctg	aggataataa	agcttgagag	780
taataatggt	aggttagcaa	aggttttagat	gtatcacttc	atgcagtcta	ccatgatagt	840
aatgcagctc	ttcgagctcat	ttctggctcat	tcaagatatt	cacctttttg	cccatagaaa	900
gcaccttacc	tcacctgctt	actgacattg	tttttagctga	tcacaagatc	attatcagcc	960
ttccattattc	cttactgtat	ataaaataca	gagttttata	ttttcctttc	ttcgtttttc	1020
accatattca	aaacctaaat	ttgtttttgc	agatggaaatg	caaagtaatc	aagtgtctgt	1080
gctttcacct	agaagggtgt	ggtcctgaag	gaaagagggtc	cctaaatatt	ccccaccctg	1140
gggtgctctc	cttccttggt	accctgacta	ccagaagtca	ggtgcttagag	cagctggaga	1200
agtgcagcag	cctgtgcttc	cacagatggg	ggtgctgctg	caacaaggct	ttcaatgtgc	1260
ccatcttagg	gggagaagct	agatcctgtg	cagcagcctg	gtaagtccctg	aggaggttcc	1320
attgctcttc	ctgctgctgt	cctttgcttc	tcaacggggc	tcgctctaca	gtctagagca	1380
catgcagcta	acttgtgcct	ctgcttatgc	atgagggtta	aattaacaac	cataaccttc	1440
atttgaagtt	caaagggtga	ttcaggatcc	tcaaagcatt	ttaaccttgc	cgcttaaaac	1500
ccaatttacc	gtgaaatggg	aattttgctg	cattgtttaa	ctgtagtgga	aacctgcta	1560
tagtaataaa	ggcttatata	gagagaaatt	gaaattaaat	gtgtttttta	atttcaaaaa	1620
aaaatcaatc	tttaggatga	cttâaaaaat	gattttgccat	gtaaaatgta	tctgcaattt	1680
ttacacaaaa	cttgttttaa	gcataaaatt	ttaaaactgt	actacttgat	gtattatata	1740
ttttgaacca	tatgttttaa	accataaaca	gtataatggt	gttataataa	aacaggcaat	1800
aaattttata	ataaaaagctg	aaaaaaaaaa	aaaaaaaaaa	aaaa		1844

<210> 89

<211> 523

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(523)

<223> n = A,T,C or G

<400> 89

tttttttttt	tttttttagt	caatccacat	ttattgatca	cttattatgt	accaggcact	60
gggataaaga	tgactgttag	tcacttcacag	taaggaagaa	aactagcaaa	taagacgatt	120
acaatatgat	gtagaaaatg	ctaagccaga	gatatagaaa	ggtcctattg	ggtccttctg	180
tcaccttgtc	tttccacatc	cctacccttc	acaggccttc	cctccagctt	cctgcccccg	240
ctccccactg	cagatcccc	gggattttgc	ctagagctaa	acgagganat	gggccccctg	300
gcccctggcat	gacttgaacc	caaccacaga	ctgggaaagg	gagcctttcg	anagtggatc	360
actttgatna	gaaaacacat	agggaaattga	agagaaantc	cccaaaggc	caccctgtgt	420
ggtgctcaag	aaaagtgtgc	agaatggata	aatgaaggat	caaggggaatt	aatanatgaa	480
taattgaatg	gtggctcaat	aagaatgact	ncnttgaatg	acc		523

<210> 90

<211> 604

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(604)

<223> n = A,T,C or G

<400> 90

ccagtgtggc	ggaatgcaaa	gattaccccc	gaagcttttcg	agaagctggg	attccctgca	60
gcaaaaggaaa	tagccaatat	gtgtcgtttc	tatgaaatga	agccagaccg	agatgtcaat	120
ctcaccacc	aactaaatcc	caaagtcaaa	agcttcagcc	agtttatctc	agagaaccag	180
gggagccttc	aagggcattg	agaaaatcag	ctgttcagat	aggcctctgc	accacacagc	240
ctctttcttc	tctgacctt	ttctcttta	cggcacaaca	ttcatgtttg	acagaacatg	300
ctggaatgca	attgtttgca	acaccgaagg	atttctctgcg	gtcgcctctt	cagttaggaag	360
cactgcattg	gtgataggac	acggttaatt	gattcacatt	taacttgcta	gttagtgata	420
aggggtggta	cacctgtttg	gtaaaatgag	aagcctcgga	aacttgggag	cttctctctt	480
accactaatg	gggagggcag	attattactg	ggatttctcc	tggggtgaat	taatttcaag	540
ccctaattgc	tgaaattccc	ctnggcaggc	tccagttttc	tcaactgcat	tgcaaaattc	600
cccc						604

<210> 91

<211> 858

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(858)

<223> n = A,T,C or G

<400> 91

tttttttttt	ttttttttta	tgattattat	tttttttatt	gatctttaca	tcttcagtgt	60
tggcagagtc	tctgatgctt	aataaacatt	tgctctgata	agataagctg	aaaaaatgt	120
catttcttta	ttcaagccat	gctttttctg	gatattctga	tcttagttga	acatacagaa	180

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ataaatgtct aaaacagcac ctcgattctc gtctataaca ggactaagtt cactgtgatc 240
ttaaataaagc ttggctaataa tgggacatga gtggaggttag tcacacttca gcgaagaaaag 300
agaatctcct gtataatctc accaggagat tcaacgaatt ccaccacact ggactagtg 360
atcccccggtg ctgcaggaat tcgatataca gcttatcgat accgtcgacc tcgagggggg 420
gcccgggtacc caattcgccc tatagtgagt cgtattacgc gcgctcactg gccgtcgttt 480
tacaacgtcg tgactgggaa aaccttggtg ttacccaact taatcgctt gcagcacatc 540
cccccttcgc cagctggcgt aatagcgaan agcccgacc gatcgccctt ncaacagttg 600
cgcagcctga atggcgaatg ggacgcgccc tgtagcggcg cattaaagcg cggcngggtg 660
tggnggntcc ccacgtgac cgntacactt ggcagcgctt tacgcccgtt ntctgctttc 720
ttcccttcct ttctcgacc gtccgcccggg ttcccccgnn agctnttaat cgggggngctc 780
cctttanggg tncnaattaa nggnttacng gaccttngan cccaaaaact ttgattaggg 840
ggaagggtccc cgaagggg 858

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<210> 92
<211> 585
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (585)
<223> n = A,T,C or G

```

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<400> 92
gttgaatctc ctggtgagat tatacaggag attctctttc ttctgtgaag tctgactacc 60
tccactcatg tcccatctta gccaaagctta tttaagatca cagtgaactt agtccctgta 120
tagacgagaa tcgaggtgct gttttagaca ttatttcttg tatgttcaac taggactaga 180
atatcacaga aaagcatggc ttgaataagg aaatgacaat tttttccact tatctgatca 240
gaacaaatgt ttattaagca tcagaaactc tgccaaactt gaggatgtaa agatcaataa 300
aaaaataaat aatcatnann naaanannan nngaagggcg gccgccaccg cgggtggagct 360
ccagcttttg ttccctttag tgagggttaa ttgcgcgctt ggcgttaact atggctatag 420
ctgtttcttg tgtgaaattg ttatccggtt cacaattccn cncaacatac gagccgggaa 480
gcntnangtg taaaagcctg ggggtgccta attgagtgag ctnactcaca ttaattngnt 540
tcgcctccac ttgcccgctt ttccantccg ggaaacctgt tcgnc 585

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<210> 93
<211> 567
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (567)
<223> n = A,T,C or G

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<400> 93
cggcagtggt gctgtctgct tgtccacact ggaatctggc tgaactggct gggaggacca 60
agactgcggc tggggtgggc anggaaggga accgggggct gctgtgaagg atcttgaac 120
ttccctgtac ccaccttccc ctgtctcat gtttgtanag gaaccttgtg ccggccaagc 180
ccagtttctt tgtgtgatac actaatgtat ttgctttttt tgggaaatan anaaaaatca 240
attaaattgc tantgtttct ttgaannnnn nnnnnnnnnn nnnnnnnngg gggngcggcc 300
cncgngnga aacnccccct ttgttccct tcaattgaaa ggttaattng cncnctggc 360
gttaanccnt gggccaaanc tngttncctg tngtgaatt gttnatccc tcccaaatc 420
cccccncc ttccaaaccc ggaaanccn anntgttna anccggggg gttgcctaan 480
ngnaattnaa ccnaaccccc nttaaatng nnttgcncn ccacngccc cnccttccca 540

```

nttcggggaa aacctntccc gtgccca

567

<210> 94
<211> 620
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(620)
<223> n = A,T,C or G

<400> 94
actagtcaaa aatgctaaaa taatttggga gaaaatattt ttttaagtagt gttatagttt 60
catgtttatc ttttattatg ttttgtgaag ttgtgtcttt tcactaatta cctatactat 120
gccaatattt ccttatatct atccataaca tttatactac atttgtaana naatatgcac 180
gtgaaactta acactttata aggtaaaaat gaggtttcca anatttaata atctgatcaa 240
gttcttgtaa tttccaaata gaatggactt ggtctgttaa gggctaagga gaagaggaag 300
ataagggttaa aagttgttaa tgaccaaaca ttctaaaaga aatgcaaaaa aaaagtttat 360
tttcaagcct tcgaactatt taaggaaagc aaaatcatth cctaaatgca tatcatttgc 420
gagaatttct cattaatatt ctgaatcatt catttcacta aggcctcatgt tnaactccgat 480
atgtctctaa gaaagtacta ttcatgggtc caaacctggt tgccatantt gggtaaaggc 540
tttcccttaa gtgtgaaant attttaaagt aaattttcct ctttttaaaa attctttana 600
agggttaagg gtgttgggga 620

<210> 95
<211> 470
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(470)
<223> n = A,T,C or G

<400> 95
ctcgaccttc tctgcacagc ggatgaacct tgagcagctg aagaccagaa aagccactat 60
nactttntgc ttaattcang agcttacang attcttcaaa gagtgngtcc agcatccttt 120
gaaacatgag ttcttaccag cagaagcaga cctttacccc accacctcag cttcaacagc 180
agcaggtgaa acaacctatc cagcctccac cttaggaaat atttgttccc acaaccaagg 240
agccatgccca ctcaaagggt ccacaacctg naaacacaaa nattccagag ccaggctgta 300
ccaagggtccc tgagccaggg ctgtaccaan gtccttgagc caggttgtag caangtccct 360
gagccaggat gtaccaaggc ccctgancca gggtgtccaa ggtccctgag ccaggctaca 420
ccaagggcct gngccaggca gcatcaangt ccctgaccaa ggcttatcaa 470

<210> 96
<211> 660
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(660)
<223> n = A,T,C or G

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<400> 96
tttttttttt tttttttttt ggaattaaaa gcaatttaat gagggcagag caggaaacat    60
gcatttccttt tcattcgaat cttcagatga accctgagca gccgaagacc agaaaagcca    120
tgaagacttt ctgcttaatt caggggctta caggattctt cagagtgtgt gtgaacaaaa    180
gctttatagt acgtattttt aggatacaaa taagagagag actatggctt ggggtgagaa    240
tgtactgatt acaagggtcta cagacaatta agacacagaa acagatggga agagggtgnc    300
cagcatctgg nggttggctt ctcaagggtt tgtctgtgca ccaaattact tctgcttggg    360
cttctgctga gctgggacctg gagtgacctg tgaaggacat ggctctggta cctttgtgta    420
gcctgncaca ggaactttgg tgtatccttg ctcaaggaaact ttgatggcac ctggctcagg    480
aaacttgatg aagccttggg caagggacct tgatgcttgc tggctcaggg accttgngn    540
ancctgggct canggacctt tgnncnaacc ttggcttcaa gggaccttg gnacatcctg    600
gcnnagggac ccttgggncc aacctggggc tttagggacc ctttggntnc nanccttggc    660

<210> 97
<211> 441
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (441)
<223> n = A,T,C or G

<400> 97
gggaccatac anagtattcc tctcttcaca ccaggaccag ccactgttgc agcatgagtt    60
cccagcagca gaagcagccc tgcattcccac cccctcagct tcagcagcag cagggtgaaac    120
agccttgcca gccctccact caggaaccat gcattcccac aaccaaggag ccttgccacc    180
ccaagggtgc tgagccctgc caccctaaaag tgcctgagcc ctgccagccc aagggtccag    240
agcctatgcca cccaagggtg cctgagccct gcccttcaat agtcactcca gcaccagccc    300
agcagaanac caagcagaag taatgtggtc cacagccatg cccttgagga gccggccacc    360
agatgctgaa tcccctatcc cattctgtgt atgagtccca ttgacctgc aattagcatt    420
ctgtctcccc caaaaaaaaaa a                                     441

<210> 98
<211> 600
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (600)
<223> n = A,T,C or G

<400> 98
gtatttcctt cttcacacca ggaccagcca ctgttgcagc atgagttccc agcagcagaa    60
gcagccctgc atcccccccc ctcagcttca gcagcagcag gtgaaacagc cttgccagcc    120
tccacctcag gaacctatga tccccaaaac caaggagccc tggcacccca aggtgcttga    180
gccctgccac cccaaaagtgc ctgagccctg ccagcccaag gttccagagc catgccacc    240
caagggtgct gagccctgcc cttcaatagt cactccagca ccagccagc agaanaccac    300
gcagaagtaa tgtggtccac agccatgccc ttgaggagcc ggcaccana tgctgaatcc    360
cctatcccat tctgtgtatg agtcccattt gccttgcaat tagcattctg tctcccccaa    420
aaaagaatgc gctatgaagc tttcttctct acacactctg agtctctgaa tgaagctgaa    480
ggcttcaant acagantag ttttcagctg ctcaagaatt cctgaagaaa agatttaaga    540
tgaaaggcaa atgattcagc tccctattac ccatttaaat tcnctttcaa tccccaaaaa    600

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<210> 99
 <211> 667
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(667)
 <223> n = A,T,C or G

<400> 99
 actagtgact gagttcctgg caaagaaatt tgacctggac cagttgataa ctcattgtttt 60
 accattttaa aaaatcagtg aaggatttga gctgctcaat tcaggacaaa gcattcgaac 120
 ggtcctgacg ttttgagatc caaagtggca ggaggtctgt gttgtcatgg tgaactggag 180
 tttctcttgt gagagttccc tcatctgaaa tcatgtatct gtctcacaaa tacaagcata 240
 agtagaagat ttgttgaaga catagaaccc ttataaagaa ttattaacct ttataaacat 300
 ttaaagtcctt gtgagcacct gggatttagt ataataacaa tgttnatatt tttgatttac 360
 attttgaag gctataattg tatcttttaa gaaaacatac cttggatttc tatgttgaaa 420
 tggagatttt taagagtttt aaccagctgc tgcagatata ttactcaaaa cagatatagc 480
 gtataaagat atagttaatg catctcctag agtaaatctt acttaacaca ttggaaacta 540
 ttatttttta gatttgaata tnaatgtrt tttttaaaca cttgttatga gttacttggg 600
 attacatttt gaaatcagtt cattccatga tgcantattc tgggattaga ttaagaaaga 660
 cggaaaa 667

<210> 100
 <211> 583
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(583)
 <223> n = A,T,C or G

<400> 100
 gttttgtttg taagatgatc acagtcattgt tacactgatc taaaggacat atatataacc 60
 ctttaaaaaa aaaatcactg cctcattctt atttcaagat gaatttctat acagactaga 120
 tgtttttctg aagatcaatt agacattttg aaaatgattt aaagtgtttt ccttaattgt 180
 ctctgaaaac aagtttcttt tgtagtttta accaaaaaag tgcccttttt gtcactggat 240
 cctcctagca ttcattgattt ttttttcata caatgaaatt aaaattgcta aaatcatgga 300
 ctggcctttt ggttggattt caggtaagat gtgtttaagg ccagagcttt tctcagtatt 360
 tgattttttt cccaatatt tgatttttta aaaatataca catnggtgct gcatttatat 420
 ctgctgggtt aaaattctgt catatttcac ttctagcctt ttagttatgg caaatcatat 480
 ttacttttta cttaaagcat ttggttattt ggantatctg gttctannct aaaaaanta 540
 attctatnaa ttgaantttt ggtactcnnc catatttgga tcc 583

<210> 101
 <211> 592
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(592)
 <223> n = A,T,C or G

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<400> 101
gtggagacgt acaaagagca gccgctcaag acacctggga agaaaaagaa aggcaagccc      60
gggaaacgca aggagcagga aaagaaaaaa cggcgaactc gctctgcctg gttagactct      120
ggagtgactg ggagtgaggc agaaggggac cacctgtctg acacctccac aacgtcgtcg      180
gagctcgatt cacggaggca ttgaaatttt cagcaganac cttccaagga catattgcag      240
gatctgtaa tagtgaacar atggaaagta ttagaaatat ttattgtctg taaatactgt      300
aaatgcattg gaataaaact gtctcccca ttgctctatg aaactgcaca ttggtcattg      360
tgaatatatt tttttttgcc aaggctaata caattattat taccacattt accataattt      420
atattgtcca ttgatgtatt tattttgtaa atgtatcttg gtgctgctga atttctatat      480
ttttgtaca taatgcnctt anatatacct atcaagtttg ttgataaatg acncaatgaa      540
gtgncncnan ttggnggttg aatttaatga atgcctaatt ttattatccc aa              592

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<210> 102
<211> 587
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (587)
<223> n = A,T,C or G

```

```

<400> 102
cgtcctaagc acttagacta catcaggga gaacacagac cacatccctg tctctatgcg      60
gcttatgttt tctggaagaa agtggagacc nagtccttg gcttagggct ccccggtg      120
gggctgtgca ntccggctcag ggcgggaagg gaaatgcacc gctgcattgt aacttacagc      180
ccaggcggat gccctctccc ttagcactac ctggcctcct gcacccccc gctctatgtt      240
cctcccacct tcaanaaatg aanaacccca tgggcccagc ccttgcccc ggggaaccaa      300
ggcagccttc caaaactcag gggtgaagc anactattag ggcaggggct gactttgggt      360
gacactgccc attccctctc agggcagctc angtcacccn ggnctcttga acccagcctg      420
ttcctttgaa aaaggggcaa actgaaaagg gcttttctta naaaaagaaa aaccagggaa      480
ctttgccagg gcttcnntnt taccaaaacn ncttctcnng gatttttaat tccccattng      540
gcctccactt accnggggcn atgccccaaa attaanaatt tcccatc              587

```

```

<210> 103
<211> 496
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (496)
<223> n = A,T,C or G

```

```

<400> 103
anaggactgg ccctacntgc tctctctcgt cctacctatc aatgcccac atggcagaac      60
ctgcancctt tggncactgc anatggaaac ctctcagtgt cttgacatca ccctaccnt      120
gcggtgggtc tccaccacaa ccactttgac tctgtgggtc ctgnanggtg gnttctcctg      180
actggcagga tggaccttan ccnacatata cctctgttcc ctctgctnag anaaagaatt      240
cccttaacat gatataatcc acccatgcaa ntngctactg gcccgactac catttaccat      300
ttgccttaga aatttcattc agtctacact ttggcattct ccttggcga agagtgtggc      360
tgggctgacc gcaaaagggt ccttacacac tggcccccac cctcaaccgt tgacncatca      420
gangcttgcc tctccttctt gattnncccc catgttggat atcagggtg tcnagggtt      480
ggaaaagaaa caaaac              496

```


<210> 104
 <211> 575
 <212> DNA
 <213> Homo sapien

 <220>
 <221> misc_feature
 <222> (1)...(575)
 <223> n = A,T,C or G

<400> 104
 gcacctgctc tcaatccnnc tctcaccatg atcctccgcc tgcanaaact cctctgccaa 50
 ctatggangt ggtttcnggg gtggctcttg ccaactggga agaagccgtg gtgtctctac 120
 ctgttcaact cngtttgtgt ctgggggata aactnggggc tatggaagcg gctnaactgt 180
 tgttttggtg gaaagggtcg taattggctt tgggaagtng cttatngaag ttggcctngg 240
 gaagtgccta ttgaaagtng ccntggaagt ngntttggtg ggggggtttg ctggtggcct 300
 ttgttnaatt tgggtgcttt gtnaatggcg gccccctcnc ctgggcaatg aaaaaaatca 360
 ccnatgcngn aaacctcnac nnaacagcct gggtctccct cacctcgaaa aaagtgcctc 420
 ccccccaaaa aaaggncan cccctcaann tgggaangttg aaaaaatcct cgaatgggga 480
 nccnnaaaac aaaaanccsc ccntttcccn gnaanggggg aaataccncc cccccactta 540
 cnaaaacccct tntaaaaaac cccccgggaa aaaaa 575

<210> 105
 <211> 619
 <212> DNA
 <213> Homo sapien

 <220>
 <221> misc_feature
 <222> (1)...(619)
 <223> n = A,T,C or G

<400> 105
 cactagtagg atagaaacac tgtgtcccga gagtaaggag agaagctact attgattaga 50
 gcctaaccac ggtaactgac aagaagaggc gggatacttt cagctttcca tgtaactgta 120
 tgcataaagc caatgtagtc cagtttctaa gatcatgttc caagctaacct gaatccact 180
 tcaatacaca ctcatgaact cctgatggaa caataacagg cccaagcctg tggatgatg 240
 tgcacacttg ctgactcan aaaaaatact actctcataa atgggtggga gtattttggt 300
 gacaacctac tttgcttggc tgagtgaagg aatgatattc atatattcat ttattccatg 360
 gacatttagt tagtgctttt tatataccag gcatgatgct gagtgacact cttgtgtata 420
 tttccaaatt tttgtacagt cgctgcacat atttgaaatc atatattaag acttccaaaa 480
 aatgaagtcc ctggtttttc atggcaactt gatcagtaaa ggattcncct ctggttggtg 540
 cttaaaaacat ctactatatn gttnanatga aattcctttt cccncctcc cgaaaaaana 600
 aagtgggtggg gaaaaaaaaa 619

<210> 106
 <211> 506
 <212> DNA
 <213> Homo sapien

 <220>
 <221> misc_feature
 <222> (1)...(506)
 <223> n = A,T,C or G

```

<400> 106
cattggtnct ttcatTTgct ntggaagtgt nnatctctaa cagtggacaa agttcccngt    60
gccttaaaact ctgtnacact tttgggaant gaaaanttng tantatgata ggttattctgt    120
angtanagat gttctggata ccattanatn tgccccngt gtcagaggct catattgtgt    180
tatgtaaagt gtatntcatt cgctactatn antcaattng aaatanggct tttgggttat    240
gaatantnng cagcncanct nanangctgt ctgtngtatt cattgtgggc atagcacctc    300
acancattgt aacctcnatc nagtgagaca nactagnaana ttcttagtga tggctcanga    360
ttccaaatgg nctcatntcn aatgtttaaa agttanttaa gtgtaagaaa tacagactgg    420
atgttccacc aactagtacc tgtaatgaen ggctgtccc aacacatctc ccttttccat    480
gactgtggta ncccgcatcg gaaaaa                                         506

```

```

<210> 107
<211> 452
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(452)
<223> n = A,T,C or G

```

```

<400> 107
gttgagctctg tactaaacag taagatatct caatgaacca taaattcaac ttgtaaaaa    60
tcttttgaag catagataat attgtttggg aaatgtttct ttgttttggc aaatgtttct    120
tttaaaagacc ctccattctt ataaaactct gcattgtagag gcttgtttac ctctctctct    180
ctaagggtta caataggagt ggtgatttga aaaatatcaa attatgagat tggttttcct    240
gtggcataaa ttgcatcact gtatcatttt cttttttaac cggtaagant tttagtttgt    300
tggaaaagtaa ctgtganaac ccagtttccc gtccatctcc cttaggggact acccatagaa    360
catgaaaagg tccccacnga agcaagaaga taagtctttc atggctgctg gttgctttaa    420
ccactttaaa accaaaaaat tccccttgga aa                                         452

```

```

<210> 108
<211> 502
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(502)
<223> n = A,T,C or G

```

```

<400> 108
atcttcttcc cttaattagt tnttatttat ntattaaatt ttattgcatg tcttgcaaaa    60
caaaaagaga ttgtagattg gcttctgggt ccccaaaagc ccataacaga aagtaccaca    120
agaccncaac tgaagcttaa aaaatctatc acatgtataa tacccttnga agaaccattaa    180
tanagcatat aaaactttta acatntgctt aatgttgtnc aattataaaa ntaatngaaa    240
aaaatgtccc tttaacatnc aatatccac atagtgttat tttaggggat taccnngnaa    300
naaaaaagg gtagaaggga tttaatgaaa actctgcttn ccatttctgt ttanaaacgt    360
ctccagaaca aaaacttntc aantctttca gctaaccgca tttagactna ggccactcaa    420
aaactccatt agnccactt tctaanggtc tctanagctt actaancctt ttgacctct    480
accctggnra ctctgcect ca                                         502

```

```

<210> 109
<211> 1302

```

<212> DNA

<213> Homo sapien

<400> 109

```

accgaggtc tcgctaaaaat catcatggat tcacttggcg ccgtcagcac tcgacttggg      60
tttgatcttt tcaaagagct gaagaaaaca aatgatggca acatcttctt ttcccttctg      120
ggcatcttga ctgcaattgg catggtcctc ctggggaccc gaggagccac cgcttcccag      180
ttggaggagg tgtttctactc tgaaaaagag acgaagagct caagaataaa ggctgaagaa      240
aaagaggtga ttgagaacac agaagcagta catcaacaat tccaaaagt tttgactgaa      300
ataagcaaac tcactaatga ttatgaactg aacataacca acaggctgtt tggagaaaaa      360
acatacctct tccttcaaaa atacttagat tatgttgaaa aatattatca tgcattctctg      420
gaacctgttg attttgtaaa tgcagccgat gaaagtcgaa agaagattaa ttcttgggtt      480
gaaagcaaaa caaatgaaaa aatcaaggac ttgttcccag atggctctat tagtagctct      540
accaagctgg tgctgggtgaa catggtttat tttaaagggc aatgggacag ggagtttaag      600
aaagaaaata ctaaggaaga gaaattttgg atgaataaga gcacaagtaa atctgtacag      660
atgatgacac agagccattc ctttagcttc actttccttg aggacttgca ggccaaaatt      720
ctagggattc catataaaaa caacgacctc agcatgtttg tgcttctgca caacgacatc      780
gatggcctgg agaagataat agataaaaata agtcctgaga aattggtaga gtggactagt      840
ccagggcata tggagaagaa aaaggtgaat ctgcacttgc cccgggttga ggtggaggac      900
agttacgata tagagcggtt cctggctgcc atggggatgg gcgatgcctt cagttagcac      960
aaagccgact actcgggaat gtcgtcaggg tccgggttgt acgccagaa gttcctgcac      1020
agttcctttg tggcagtaac tgaggaaggg accgaggctg cagctgccac tggcataggc      1080
tttactgtca catccgcccc aggtcatgaa aatgttcaat gcaatcatcc ctctctgttc      1140
ttcatcaggg acaatgaatc caacagcatc ctcttcttcg gcagattttc ttctccttaa      1200
gatgatcgtt gccatggcat tgctgctttt agcaaaaaac aactaccagt gtactcata      1260
tgattatgaa aatcgtccat tcttttaaat ggtggctcac tcgcattt      1308

```

<210> 110

<211> 391

<212> PRT

<213> Homo sapien

<400> 110

```

Met Asp Ser Leu Gly Ala Val Ser Thr Arg Leu Gly Phe Asp Leu Phe
 1          5          10          15
Lys Glu Leu Lys Lys Thr Asn Asp Gly Asn Ile Phe Phe Ser Pro Val
          20          25          30
Gly Ile Leu Thr Ala Ile Gly Met Val Leu Leu Gly Thr Arg Gly Ala
          35          40          45
Thr Ala Ser Gln Leu Glu Glu Val Phe His Ser Glu Lys Glu Thr Lys
          50          55          60
Ser Ser Arg Ile Lys Ala Glu Glu Lys Glu Val Ile Glu Asn Thr Glu
65          70          75          80
Ala Val His Gln Gln Phe Gln Lys Phe Leu Thr Glu Ile Ser Lys Leu
          85          90          95
Thr Asn Asp Tyr Glu Leu Asn Ile Thr Asn Arg Leu Phe Gly Glu Lys
100          105          110
Thr Tyr Leu Phe Leu Gln Lys Tyr Leu Asp Tyr Val Glu Lys Tyr Tyr
115          120          125
His Ala Ser Leu Glu Pro Val Asp Phe Val Asn Ala Ala Asp Glu Ser
130          135          140
Arg Lys Lys Ile Asn Ser Trp Val Glu Ser Lys Thr Asn Glu Lys Ile
145          150          155          160
Lys Asp Leu Phe Pro Asp Gly Ser Ile Ser Ser Ser Thr Lys Leu Val
          165          170          175

```

Leu Val Asn Met Val Tyr Phe Lys Gly Gln Trp Asp Arg Glu Phe Lys
 180 185 190
 Lys Glu Asn Thr Lys Glu Glu Lys Phe Trp Met Asn Lys Ser Thr Ser
 195 200 205
 Lys Ser Val Gln Met Met Thr Gln Ser His Ser Phe Ser Phe Thr Phe
 210 215 220
 Leu Glu Asp Leu Gln Ala Lys Ile Leu Gly Ile Pro Tyr Lys Asn Asn
 225 230 235 240
 Asp Leu Ser Met Phe Val Leu Leu Pro Asn Asp Ile Asp Gly Leu Glu
 245 250 255
 Lys Ile Ile Asp Lys Ile Ser Pro Glu Lys Leu Val Glu Trp Thr Ser
 260 265 270
 Pro Gly His Met Glu Glu Arg Lys Val Asn Leu His Leu Pro Arg Phe
 275 280 285
 Glu Val Glu Asp Ser Tyr Asp Leu Glu Ala Val Leu Ala Ala Met Gly
 290 295 300
 Met Gly Asp Ala Phe Ser Glu His Lys Ala Asp Tyr Ser Gly Met Ser
 305 310 315 320
 Ser Gly Ser Gly Leu Tyr Ala Gln Lys Phe Leu His Ser Ser Phe Val
 325 330 335
 Ala Val Thr Glu Glu Gly Thr Glu Ala Ala Ala Thr Gly Ile Gly
 340 345 350
 Phe Thr Val Thr Ser Ala Pro Gly His Glu Asn Val His Cys Asn His
 355 360 365
 Pro Phe Leu Phe Phe Ile Arg His Asn Glu Ser Asn Ser Ile Leu Phe
 370 375 380
 Phe Gly Arg Phe Ser Ser Pro
 385 390

<210> 111
 <211> 1419
 <212> DNA
 <213> Homo sapien

<400> 111
 ggagaactat aaattaagga tcccagctac ttaattgact tatgcttcct agttcgttgc 60
 ccagccacca cgcctctctc aaaaaccgga ggtctcgcta aaatcatcat ggattcactt 120
 ggcgccgtca gactctgact tgggtttgat cttttcaaag agctgaagaa aacaaatgat 180
 ggcaacatct tcttttcccc tgtgggcac ttgactgcaa ttggcatggt cctcctgggg 240
 acccgaggag ccaccgcttc ccagttggag gaggtgttct actctgaaaa agagacgaag 300
 agctcaagaa taaaggctga agaaaaagag gtggtaagaa taaaggctga aggaaaagag 360
 atrgagaaca cagaagcagt acatcaacaa ttccaaaagt ttttgactga aataagcaaa 420
 ctactaatg attatgaact gaacataacc aacaggctgt ttggagaaaa aacatacctc 480
 ttccttcaaa aatacttaga ttatgttgaa aaatattatc atgcatctct ggaacctgtt 540
 gattttgtaa atgcagccga tgaaagtcga aagaagatta attcctgggt tgaaagcaaa 600
 acaaatgaaa aaatcaagga cttgttccca gatggctcta ttagtagctc taccaagctg 660
 gtgctggtga acatggttta ttttaaaggg caatgggaca gggagttaa gaaagaaaat 720
 actaaggaag agaaattttg gatgaataag agcacaagta aatctgtaca gatgatgaca 780
 cagagccatt cctttagctt cactttctctg gaggacttgc aggccaaaat tctagggatt 840
 ccataataaa acaacgacct aagcatgttt gtgcttctgc ccaacgacat cgatggcctg 900
 gagaagataa tagataaaat aagtcctgag aaattggtag agtggactag tccagggcat 960
 atggaagaaa gaaagggtgaa tctgcacttg ccccggtttg aggtggagga cagttacgat 1020
 cttagggcgg tcttggtctg catggggatg ggcgatgcct tcagttagca caaagccgac 1080
 tactcgggaa tgcgtcagg ctccgggttg tacgccaga agttcctgca cagttccttt 1140
 gtggcagtaa ctgaggaagg caccgaggct gcagctgcca ctggcatagg ctttactgtc 1200

```

acatccgcc caggtcatga aaatgttcac tgcaatcatc ccttcctggt cttcatcagg 1260
cacaatgaat ccaacagcat cctcttcttc gccagatttc cttctcctta agatgatcgt 1320
tgccatggca ttgctgcttt tagcaaaaaa caactaccag tgttactcat atgattatga 1380
aaatcgcca ttcttttaaa tggtaggctca ctgcatatt 1419

```

```

<210> 112
<211> 400
<212> PRT
<213> Homo sapien

```

```

<400> 112
Met Asp Ser Leu Gly Ala Val Ser Thr Arg Leu Gly Phe Asp Leu Phe
1 5 10 15
Lys Glu Leu Lys Lys Thr Asn Asp Gly Asn Ile Phe Phe Ser Pro Val
20 25 30
Gly Ile Leu Thr Ala Ile Gly Met Val Leu Leu Gly Thr Arg Gly Ala
35 40 45
Thr Ala Ser Gln Leu Glu Glu Val Phe His Ser Glu Lys Glu Thr Lys
50 55 60
Ser Ser Arg Ile Lys Ala Glu Glu Lys Glu Val Val Arg Ile Lys Ala
65 70 75 80
Glu Gly Lys Glu Ile Glu Asn Thr Glu Ala Val His Gln Gln Phe Gln
85 90 95
Lys Phe Leu Thr Glu Ile Ser Lys Leu Thr Asn Asp Tyr Glu Leu Asn
100 105 110
Ile Thr Asn Arg Leu Phe Gly Glu Lys Thr Tyr Leu Phe Leu Gln Lys
115 120 125
Tyr Leu Asp Tyr Val Glu Lys Tyr Tyr His Ala Ser Leu Glu Pro Val
130 135 140
Asp Phe Val Asn Ala Ala Asp Glu Ser Arg Lys Lys Ile Asn Ser Trp
145 150 155 160
Val Glu Ser Lys Thr Asn Glu Lys Ile Lys Asp Leu Phe Pro Asp Gly
165 170 175
Ser Ile Ser Ser Ser Thr Lys Leu Val Leu Val Asn Met Val Tyr Phe
180 185 190
Lys Gly Gln Trp Asp Arg Glu Phe Lys Lys Glu Asn Thr Lys Glu Glu
195 200 205
Lys Phe Trp Met Asn Lys Ser Thr Ser Lys Ser Val Gln Met Met Thr
210 215 220
Gln Ser His Ser Phe Ser Phe Thr Phe Leu Glu Asp Leu Gln Ala Lys
225 230 235 240
Ile Leu Gly Ile Pro Tyr Lys Asn Asn Asp Leu Ser Met Phe Val Leu
245 250 255
Leu Pro Asn Asp Ile Asp Gly Leu Glu Lys Ile Ile Asp Lys Ile Ser
260 265 270
Pro Glu Lys Leu Val Glu Trp Thr Ser Pro Gly His Met Glu Glu Arg
275 280 285
Lys Val Asn Leu His Leu Pro Arg Phe Glu Val Glu Asp Ser Tyr Asp
290 295 300
Leu Glu Ala Val Leu Ala Ala Met Gly Met Gly Asp Ala Phe Ser Glu
305 310 315 320
His Lys Ala Asp Tyr Ser Gly Met Ser Ser Gly Ser Gly Leu Tyr Ala
325 330 335
Gln Lys Phe Leu His Ser Ser Phe Val Ala Val Thr Glu Glu Gly Thr
340 345 350

```

Glu Ala Ala Ala Ala Thr Gly Ile Gly Phe Thr Val Thr Ser Ala Pro
 355 360 365
 Gly His Glu Asn Val His Cys Asn His Pro Phe Leu Phe Phe Ile Arg
 370 375 380
 His Asn Glu Ser Asn Ser Ile Leu Phe Phe Gly Arg Phe Ser Ser Pro
 385 390 395 400

<210> 113
 <211> 957
 <212> DNA
 <213> Homo sapien

<400> 113
 ctgcaccttc tctgcacagc ggatgaaccc tgagcagctg aagaccagaa aagccactat 60
 gactttctgc ttaattcagg agcttacagg attcttcaaa gagggtgtcc agcatctctt 120
 gaaacatgag ttcttaccag cagaagcaga cctttacccc accacctcag cttcaacagc 130
 agcaggtgaa acaacccagc cagcctccac ctcaggaaat atttggtccc acaaccaagg 240
 agccatgcca ctcaaaaggtt ccacaacctg gaaacacaaa gatccagag ccaggctgta 300
 ccaaggtccc tgagccaggc tgtaccaagg tccctgagcc aggttgtacc aaggtccctg 360
 agccaggatg taccaagggtc cctgagccag gttgtaccaa ggtccctgag ccaggctaca 420
 ccaaggtccc tgagccaggc agcatcaagg tccctgacca aggttctatc aagtttctg 480
 agccaggtgc catcaaaagt cctgagcaag gatacaccaa agttccctgt ccaggctaca 540
 caaaggtacc agagccatgt cttcaacgg tcactccagg cccagctcag cagaagacca 600
 agcagaagta atttggtgca cagacaagcc cttgagaagc caaccaccag atgctggaca 660
 cctctctccc atctgtttct gtgtcttaat tgtctgtaga ccttgtaacc agtacattct 720
 caccccaagc catagtctct ctcttatttg tatcttaaaa atacgggtact ataaagcttt 780
 tgttcacaca caactctgaag aatcctgtaa gccctgaat taagcagaaa gtcttcattg 840
 cttttctgggt cttcggtctc tcagggttca tctgaagatt cgaatgaaaa gaaatgcctg 900
 tttctctgctc tgccttcatt aaattgcttt taattccaaa aaaaaaaaaa aaaaaaa 957

<210> 114
 <211> 161
 <212> PRT
 <213> Homo sapien

<400> 114
 Met Ser Ser Tyr Gln Gln Lys Gln Thr Phe Thr Pro Pro Pro Gln Leu
 1 5 10 15
 Gln Gln Gln Gln Val Lys Gln Pro Ser Gln Pro Pro Pro Gln Glu Ile
 20 25 30
 Phe Val Pro Thr Thr Lys Glu Pro Cys His Ser Lys Val Pro Gln Pro
 35 40 45
 Gly Asn Thr Lys Ile Pro Glu Pro Gly Cys Thr Lys Val Pro Glu Pro
 50 55 60
 Gly Cys Thr Lys Val Pro Glu Pro Gly Cys Thr Lys Val Pro Glu Pro
 65 70 75 80
 Gly Cys Thr Lys Val Pro Glu Pro Gly Cys Thr Lys Val Pro Glu Pro
 85 90 95
 Gly Tyr Thr Lys Val Pro Glu Pro Gly Ser Ile Lys Val Pro Asp Gln
 100 105 110
 Gly Phe Ile Lys Phe Pro Glu Pro Gly Ala Ile Lys Val Pro Glu Gln
 115 120 125
 Gly Tyr Thr Lys Val Pro Val Pro Gly Tyr Thr Lys Val Pro Glu Pro
 130 135 140
 Cys Pro Ser Thr Val Thr Pro Gly Pro Ala Gln Gln Lys Thr Lys Gln

145
Lys

150

155

160

<210> 115
 <211> 506
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (506)
 <223> n = A,T,C or G

<400> 115
 cattggtnct ttcatttgct ntgggaagtgt nnatctctaa cagtggacaa agttcccngt 60
 gccctaaact ctgtnacact tttgggaant gaaaanttnng tantatgata ggttattctg 120
 angrnagat gttctggata ccattanatn tgccccngt gtcagaggc catatttgrt 180
 tatgtaaatg gtatntcatt cgctactatn antcaattng aaatanggct tttgggttat 240
 gaatanntng cagcncancn nanangctgt ctgtngtatt cattgtggct atagcacctc 300
 acancattgt aacctcnatc nagtgagaca nactagnaan ttccatgtga tggctcanga 360
 ttccaaatgg nctcatntcn aatgtttraaa agttanttaa gtgtaagaaa tacagactgg 420
 atgttccacc aactagtacc tgtaatgacn ggctgtgtcc aacacatctc ccttttccat 480
 gactgtggta ncccgcacg gaaaaa 506

<210> 116
 <211> 3079
 <212> DNA
 <213> Homo sapien

<400> 116
 ggatccccgg gtttctctaaa cccccacag agtcttgccc aggccaaaga gcaaggaaaa 60
 ggtcaaaagg cagaaaaaat gctgagttag gaggagctat ggaaggataa acctggcctc 120
 aaagaggtca aagtgtctta tagggggcgc tgagggtctc ccacattctc tggcctaaac 180
 ctgtcaggca gatctgcccc gtgggtctctg ggatagctgt gccttcctca acaaaaaaat 240
 tgtgcacaaa aggatgaaac tctattttcc ctctagcaca taaccaagaa tataaggcta 300
 cagattgcct tcccagagg gaaaacctg cagcaacctg ctgcctggaa aagtgtgaaga 360
 gcagatcact ggggaatcgt ttgcccccg ctgatggaca gcttcccaa gctccaaggg 420
 cagggtgctca gcatgtaccg tactgggatg gttgtcaata ctctgtgtcc tgaagagtc 480
 ccaggacact gccatgcca tgccccctca gttcctggca tcttttttg gctgctcaca 540
 gccccagcct ctatggtgaa gacatacttg ctgacagcgt caccacttg ttgccaagag 600
 atcagtgtct gaaggcaagg ttatttctaa ctgagcagag cctgccagga agaaagcgt 660
 tgcacccac accactgtgc aggtgtgacc ggtgagctca cagctgccc ccaggcatgc 720
 ccagccact taatcatcac agctcgacag ctctctcgcc cagcccagtt ctggaaggga 780
 caaaaagggg catcaccgtt cctgggtaac agagccacct tctgcgtcct gctgagctct 840
 gttctctcca gcacctcca accactagt gcctggttct ctgctccac caggaaacaag 900
 ccaccatgtc tggccagtca agtgtgtctt ccggagcggg gggcagtcgt agcttcagca 960
 ccgctctgc catcaccgg tctgtctccc gcaccagctt cactccgtg tcccggctcg 1020
 ggggtggcgg tgggtgtggc ttccggcagg tcagccttgc ggggtgctgt ggaagtggcg 1080
 gctatggcag ccggagcctc tacaacctgg ggggtctcaa gaggatatcc atcagcacta 1140
 gtggtggcag cttcaggaac cggtttggcg ctggtgctgg aggcggctat ggctttggag 1200
 gtggtgcccg tagtggattt ggtttcggcg gtggagctgg tgggtggctt gggctcggcg 1260
 gcggagctgg ctttggaggc ggcttcggcg gccctggctt tctgtctgc cctcctggag 1320
 gtatccaaga ggtcactgtc aaccagagtc tcttgactcc cctcaacctg caaatcgacc 1380
 ccagcatcca gaggggtgagg accgaggagc gcgagcagat caagacctc aacaataagc 1440

ttgcctcctt	catcgacaag	gtgcgggtcc	tggagcagca	gaacaagggt	ctggaaacaa	1500
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8948

<210> 120
 <211> 587
 <212> DNA
 <213> Homo sapien
 <220>
 <221> misc_feature
 <222> (1)...(587)
 <223> n = A,T,C or G

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<210> 121
 <211> 619
 <212> DNA
 <213> Homo sapien
 <220>
 <221> misc_feature
 <222> (1)...(619)
 <223> n = A,T,C or G

<400> 121
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 aatgaagtcc ctggtttttc atggcaactt gatcagtaaa ggattcncct ctgtttggta 540
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<210> 122
 <211> 1475
 <212> DNA
 <213> Homo sapien

<400> 122
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<210> 123

<211> 2254

<212> DNA

<213> Homo sapien

<400> 123

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<210> 124
<211> 956
<212> DNA
<213> Homo sapien

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<400> 124
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<210> 125
<211> 486
<212> DNA
<213> Homo sapien

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<220>
<221> misc_feature
<222> (1)...(486)
<223> n = A,T,C or G

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<400> 125
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<210> 126
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<212> DNA
<213> Homo sapien

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<210> 127

<211> 754

<212> DNA

<213> Homo sapien

<400> 127

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<210> 128

<211> 374

<212> DNA

<213> Homo sapien

<400> 128

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<210> 129

<211> 546

<212> DNA

<213> Homo sapien

<400> 129

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<211> 5155

<212> DNA

<213> Homo sapien

<400> 130

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<210> 131

<211> 671

<212> DNA

<213> Hcma sapien

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<210> 132
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<210> 133
 <211> 581
 <212> DNA
 <213> Homo sapien

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 <211> 4797
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature

<222> (1) ... (4797)

<223> n = A, T, C or G

<400> 134

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<210> 135

<211> 2956

<212> DNA

<213> Homo sapien

<400> 135

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<210> 136
 <211> 356
 <212> DNA
 <213> Homo sapien

```

<400> 136
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aggcattgat gatgatgaag attttatctc cagcaccatt tcaaccacac caggggcttt 120
tgaccacaca aaacagaacc aggactggac tcagtggaac ccaagccatt caaatccgga 180
agtgtacttt cagacaacca caaggatgac tgatgtagac agaaatggca ccactgctta 240
tgaaggaaac tggaaaccag aagcacaccc tccctcatt caccatgagc atcatgagga 300
agaagagacc ccacattcta caagcacaat ccaggcaact cctagtagta caacgg 356

```

<210> 137
 <211> 356
 <212> DNA
 <213> Homo sapien

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<220>
<221> misc_feature
<222> (1)...(356)
<223> n = A,T,C or G

<400> 137
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gtcactggct gcccccgaa cagggcgctg ctccatggct ctgcttgtgg tagtctgtgg 120
ctatgtctcc cagcaaggac agaaactcag aaaaatcaat ctcttctatcc tcattcttgt 180
cctttttctc aaagacatcg gcgaggtaat ttgtgccctt ttacctcgg ccgcgacca 240
cgctaaggcc aaanttcag acanayggcc gggccggtnc nataggggan cccaacttgg 300
ggacccaaac tctggcgcgg aaacacangg gcataagctt gnttcctgtg gggaaa 356

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<210> 138
 <211> 353
 <212> DNA
 <213> Homo sapien

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<400> 138
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tacattgatg tggaaattgc tgctgctacc accacctcct gaagaggctt cctgatgccc 180
aatgccagcc atcttggcat cctggccctc gaggaggctg cggtaagtag cgatctcctg 240
ctccagccgt gtctttatgt caagcagcat cttgtactcc tggttctgag cctccatctc 300
gcacccgagc tcaactcagac ctccgscgsg mssmcgctam gccgaattcc agc 353

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<210> 139
 <211> 371
 <212> DNA
 <213> Homo sapien

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<400> 139
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agacatatcc tacacttcaa agctttgggtg caattcccat cgaccagagt tggcccgacc 120
agccttggaa aggtcactga aaaatcttca attggattat gttgaccttc acctattca 180
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actatttgac acagtggatc tctgtgccac gtgggaggcc gtggagaagt gtaaaagatgc 300
aggattggac ctgcccgggc ggccgctcga aagccgaatt ccagcacact ggcggccggt 360
actagtggat c 371

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<210> 140
 <211> 370
 <212> DNA
 <213> Homo sapien

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<400> 140
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tgggagccag ggcagatggt gcattccttt gtgtccctgt aaatgtggga ctacaagaag 120
aggagctgcc tgagtggtag tttctcttcc tggtaatcct ctggcccagc ctcatggcag 180
aatagaggta tttttaggct atttttgtaa tatggcttct ggtcaaaatc cctgtgtagc 240
tgaattccca agccctgcat tgtacagccc cccactcccc tcaccaccta ataaaggaat 300
agttaacact caaaaaaaaa aaaaaacctg cccggggcggc cgctcgaaag ccgaattcca 360
gcacactggc 370

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<210> 141
 <211> 371
 <212> DNA
 <213> Homo sapien

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<400> 141
tagcgtggct gcggccgagg tctctctgtc tgcctgtcac agcccgatgg taccagcgca 60
gggtgtaggc agtgcaggag cctcatcca grggcaggga acaggggtca tcactatccc 120

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aaggagcttc agggtcctgg tactcctcca cagaatactc ggagtattca gagtactcat 180
catcctcagg gggtagccgc tcttcctcct ctgcatgaga gacgcggagc acaggcacag 240
carggagctg ggagccggca gtgtctgcag cataactagg gaggggtcgt gatccagatg 300
cgatgaactg gccctggcag gcacagtgtc gactcatctc ttggcgacct gcccgggcgg 360
ccgctcgaag c 371

```

```

<210> 142
<211> 343
<212> DNA
<213> Homo sapien

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<400> 142
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tctttgggat gtgggcattc aaccacaga ggagaacttc atttgataga gcagttttga 300
aacacccttt ttgtagaatc tacaggtgga ctttagagt gct 343

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<210> 143
<211> 354
<212> DNA
<213> Homo sapien

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<400> 143
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agcaaatctc catactgttt ctttcttttt tttttcatca ctgtgttcaa ttatctttat 300
cataaacatt ttacatgcag ctatttcaaa gtgtgttga ttaattagga tcat 354

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```

<210> 144
<211> 353
<212> DNA
<213> Homo sapien

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<400> 144
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gaaacatgc cccagagaag gttaagtgc ttcctcttta tggagccagt gttccaacct 300
aggtttgctt gataccagac ctgtggcccc acctcccatg caggtctctg tgg 353

```

```

<210> 145
<211> 371
<212> DNA
<213> Homo sapien

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<400> 145
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attgccactg ttgattacta gctttttctt ctgccacac tttcttcgac tgttgactgc 180
aatgcaaaact gcaagaatca aagccaaggc caagagggat gccaaagatga tcagccattc 240

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tggaatttgg	ggtgtcctta	taggaccaga	ggttgtgttt	gctccacctt	cttgactccc	300
atgtgagacc	tcggccgcga	ccacgctaag	ccgaattcca	gcacactggc	ggcccgttac	360
tagtggatcc	g					371

<210> 146
 <211> 355
 <212> DNA
 <213> Homo sapien

<400> 146						
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cgagagcaag	ctctataaga	ttcttcaagg	tggggttggc	atccccca	tacgggtgta	300
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<210> 147
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 <212> DNA
 <213> Homo sapien

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cttttcccat	aatatgggaa	atatttttaag	tctatcatcc	cattatgagg	ataaactgct	300
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<210> 148
 <211> 369
 <212> DNA
 <213> Homo sapien

<400> 148						
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atgtggcagc	ccctctctct	caagtggctc	ttgtcctgtt	gccctgggag	ttctcaaatt	240
gctgcagcag	cctccatcca	gcctgaggat	gacatcaata	cacagaggaa	gaagagtcag	300
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acttcttcca						369

<210> 149
 <211> 620
 <212> DNA
 <213> Homo sapien

<220>
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 <222> (1...620)
 <223> n = A,T,C or G

<400> 149

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gccaatat	ctttatatct	atccataaca	tttatactac	atttgaana	naatatgcac	180
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 <212> DNA
 <213> Homo sapien

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<210> 151
 <211> 4655
 <212> DNA
 <213> Homo sapien

<400> 151						
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<210> 152
 <211> 586
 <212> PRT
 <213> Homo sapien

<400> 152
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 20 25 30
 Gly Ser Ser Ser Thr Ser Pro Tyr Asn Thr Asp His Ala Gln Asn Ser
 35 40 45
 Val Thr Ala Pro Ser Pro Tyr Ala Gln Pro Ser Ser Thr Phe Asp Ala
 50 55 60
 Leu Ser Pro Ser Pro Ala Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro
 65 70 75 80
 His Ser Phe Asp Val Ser Phe Gln Gln Ser Ser Thr Ala Lys Ser Ala
 85 90 95
 Thr Trp Thr Tyr Ser Thr Glu Leu Lys Lys Leu Tyr Cys Gln Ile Ala
 100 105 110
 Lys Thr Cys Pro Ile Gln Ile Lys Val Met Thr Pro Pro Gln Gly
 115 120 125
 Ala Val Ile Arg Ala Met Pro Val Tyr Lys Lys Ala Glu His Val Thr
 130 135 140
 Glu Val Val Lys Arg Cys Pro Asn His Glu Leu Ser Arg Glu Phe Asn
 145 150 155 160
 Glu Gly Gln Ile Ala Pro Ser Ser His Leu Ile Arg Val Glu Gly Asn
 165 170 175
 Ser His Ala Gln Tyr Val Glu Asp Pro Ile Thr Gly Arg Gln Ser Val
 180 185 190
 Leu Val Pro Tyr Glu Pro Pro Gln Val Gly Thr Glu Phe Thr Thr Val
 195 200 205
 Leu Tyr Asn Phe Met Cys Asn Ser Ser Cys Val Gly Gly Met Asn Arg
 210 215 220
 Arg Pro Ile Leu Ile Ile Val Thr Leu Glu Thr Arg Asp Gly Gln Val
 225 230 235 240
 Leu Gly Arg Arg Cys Phe Glu Ala Arg Ile Cys Ala Cys Pro Gly Arg
 245 250 255
 Asp Arg Lys Ala Asp Glu Asp Ser Ile Arg Lys Gln Gln Val Ser Asp
 260 265 270
 Ser Thr Lys Asn Gly Asp Gly Thr Lys Arg Pro Phe Arg Gln Asn Thr
 275 280 285
 His Gly Ile Gln Met Thr Ser Ile Lys Lys Arg Arg Ser Pro Asp Asp
 290 295 300
 Glu Leu Val Tyr Leu Pro Val Arg Gly Arg Glu Thr Tyr Glu Met Leu
 305 310 315 320
 Val Lys Ile Lys Glu Ser Leu Glu Leu Met Gln Tyr Leu Leu Gln His
 325 330 335
 Thr Ile Glu Thr Tyr Arg Gln Gln Gln Gln Gln His Gln His Leu
 340 345 350
 Leu Gln Lys Gln Thr Ser Ile Gln Ser Pro Ser Ser Tyr Gly Asn Ser
 355 360 365
 Ser Pro Pro Leu Asn Lys Met Asn Ser Met Asn Lys Leu Pro Ser Val
 370 375 380

Ser Gln Leu Ile Asn Pro Gln Gln Arg Asn Ala Leu Thr Pro Thr Thr
 385 390 395 400
 Ile Pro Asp Gly Met Gly Ala Asn Ile Pro Met Met Gly Thr His Met
 405 410 415
 Pro Met Ala Gly Asp Met Asn Gly Leu Ser Pro Thr Gln Ala Leu Pro
 420 425 430
 Pro Pro Leu Ser Met Pro Ser Thr Ser His Cys Thr Pro Pro Pro
 435 440 445
 Tyr Pro Thr Asp Cys Ser Ile Val Ser Phe Leu Ala Arg Leu Gly Cys
 450 455 460
 Ser Ser Cys Leu Asp Tyr Phe Thr Thr Gln Gly Leu Thr Thr Ile Tyr
 465 470 475 480
 Gln Ile Glu His Tyr Ser Met Asp Asp Leu Ala Ser Leu Lys Ile Pro
 485 490 495
 Glu Gln Phe Arg His Ala Ile Trp Lys Gly Ile Leu Asp His Arg Gln
 500 505 510
 Leu His Glu Phe Ser Ser Pro Ser His Leu Leu Arg Thr Pro Ser Ser
 515 520 525
 Ala Ser Thr Val Ser Val Gly Ser Ser Glu Thr Arg Gly Glu Arg Val
 530 535 540
 Ile Asp Ala Val Arg Phe Thr Leu Arg Gln Thr Ile Ser Phe Pro Pro
 545 550 555 560
 Arg Asp Glu Trp Asn Asp Phe Asn Phe Asp Met Asp Ala Arg Arg Asn
 565 570 575
 Lys Gln Gln Arg Ile Lys Glu Glu Gly Glu
 580 585

<210> 153
 <211> 2007
 <212> DNA
 <213> Homo sapien.

<400> 153
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<210> 154

<211> 2148

<212> DNA

<213> Homo sapien

<400> 154

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<210> 155
 <211> 153
 <212> PRT
 <213> Homo sapien

<400> 155
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 Trp Arg Pro Val Lys Ala Ser Asp Gly Asp Tyr Tyr Thr Leu Ala Val
 20 25 30
 Pro Met Gly Asp Val Pro Met Asp Gly Ile Ser Val Ala Asp Ile Gly
 35 40 45
 Ala Ala Val Ser Ser Ile Phe Asn Ser Pro Glu Glu Phe Leu Gly Lys
 50 55 60
 Ala Val Gly Leu Ser Ala Glu Ala Leu Thr Ile Gln Gln Tyr Ala Asp
 65 70 75 80
 Val Leu Ser Lys Ala Leu Gly Lys Glu Val Arg Asp Ala Lys Ile Thr
 85 90 95
 Pro Glu Ala Phe Glu Lys Leu Gly Phe Pro Ala Ala Lys Glu Ile Ala
 100 105 110
 Asn Met Cys Arg Phe Tyr Glu Met Lys Pro Asp Arg Asp Val Asn Leu
 115 120 125
 Thr His Gln Leu Asn Pro Lys Val Lys Ser Phe Ser Gln Phe Ile Ser
 130 135 140
 Glu Asn Gln Gly Ala Phe Lys Gly Met
 145 150

<210> 156
 <211> 128
 <212> PRT
 <213> Homo sapien

<400> 156
 Met Thr Ser Val Arg Val Ala Ala Tyr Phe Glu Asn Phe Leu Ala Ala
 1 5 10 15
 Trp Arg Pro Val Lys Ala Ser Asp Gly Asp Tyr Tyr Thr Leu Ala Val
 20 25 30
 Pro Met Gly Asp Val Pro Met Asp Gly Ile Ser Val Ala Asp Ile Gly
 35 40 45
 Ala Ala Val Ser Ser Ile Phe Asn Ser Pro Glu Glu Phe Leu Gly Lys
 50 55 60
 Ala Val Gly Leu Ser Ala Glu Ala Leu Thr Ile Gln Gln Tyr Ala Asp
 65 70 75 80
 Val Leu Ser Lys Ala Leu Gly Lys Glu Val Arg Asp Ala Lys Thr Ile
 85 90 95
 Cys Ala Ile Asp Asp Gln Lys Thr Val Glu Glu Gly Phe Met Glu Asp
 100 105 110
 Val Gly Leu Ser Trp Ser Leu Arg Glu His Asp His Val Ala Gly Ala
 115 120 125

<210> 157
 <211> 424
 <212> DNA
 <213> Homo sapien

<220>
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 tattagattt ccttgatgc aaagtttttg ttgaaagctg tgctcagagg aggtgagagg 240
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 agcccagaaa ctctctctgc gnatctggct tgtccatctg gtctaagggt gctgctctct 360
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 tgct 424

<210> 158
 <211> 2099
 <212> DNA
 <213> Homo sapien

<400> 158
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 aaggcacttc ctgtcgggtga agaagacctg tctcgggtgc caggggcctc ctgtcttctg 240
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 attgacattc gtatcatcac tgtgaccat tggcttctag gcaactcagt ggggtaggag 480
 aaggaggtct gaaaacctcg cagagggatc ttgcccctat tctttgggtc tgaaacactg 540
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 atcttcatct tccagatcat gatcctctg gtggctgccc aggaagtgtg ggggtgacg 720
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cggaacagtg tggaagcaga aggcctttttt aactcatccg ttgccaatc attgcaaaca 2040
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<210> 159
<211> 291
<212> PRT
<213> Homo sapien

<400> 159
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Val Met Ile Leu Val Val Ala Ala Gln Glu Val Trp Gly Asp Glu Gln
35 40 45
Glu Asp Phe Val Cys Asn Thr Leu Gln Pro Gly Cys Lys Asn Val Cys
50 55 60
Tyr Asp His Phe Phe Pro Val Ser His Ile Arg Leu Trp Ala Leu Gln
65 70 75 80
Leu Ile Phe Val Ser Thr Pro Ala Leu Leu Val Ala Met His Val Ala
85 90 95
Tyr Tyr Arg His Glu Thr Thr Arg Lys Phe Arg Arg Gly Glu Lys Arg
100 105 110
Asn Asp Phe Lys Asp Ile Glu Asp Ile Lys Lys Gln Lys Val Arg Ile
115 120 125
Glu Gly Ser Leu Trp Trp Thr Tyr Thr Ser Ser Ile Phe Phe Arg Ile
130 135 140
Ile Phe Glu Ala Ala Phe Met Tyr Val Phe Tyr Phe Leu Tyr Asn Gly
145 150 155 160
Tyr His Leu Pro Trp Val Leu Lys Cys Gly Ile Asp Pro Cys Pro Asn
165 170 175
Leu Val Asp Cys Phe Ile Ser Arg Pro Thr Glu Lys Thr Val Phe Thr
180 185 190
Ile Phe Met Ile Ser Ala Ser Val Ile Cys Met Leu Leu Asn Val Ala
195 200 205
Glu Leu Cys Tyr Leu Leu Leu Lys Val Cys Phe Arg Arg Ser Lys Arg
210 215 220
Ala Gln Thr Gln Lys Asn His Pro Asn His Ala Leu Lys Glu Ser Lys
225 230 235 240
Gln Asn Glu Met Asn Glu Leu Ile Ser Asp Ser Gly Gln Asn Ala Ile
245 250 255
Thr Gly Ser Gln Ala Lys His Phe Lys Val Lys Cys Ser Cys Val Ile
260 265 270
Arg Arg Leu Leu Ser Ser Pro Glu Gly Asn Thr Asn Leu Lys Val Pro
275 280 285
Ser Val Ala
290

<210> 160
<211> 3951
<212> DNA
<213> Homo sapien

<400> 160
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gaacctcatc	tcaaacatta	aggaaatgat	aactgaagct	tcattttacc	tatttaatgc	300
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tatgaagccc ctaatgcaaa gctctttacc tcttgctatt ttgttatata tattacagat 3420
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caaggaaata aaaatcatct ttcacttcta attttactcc ttcctcttat ttttttaaaa 3900
gattatcgaa caataaaatc atttgccttt ttaattaaaa acataaaaaa a 3951

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<210> 161

<211> 943

<212> PRT

<213> Hcmo sapien

<400> 161

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20     25     30
Val Gln Leu Gln Asp Asn Gly Tyr Asn Gly Leu Leu Ile Ala Ile Asn
35     40     45
Pro Gln Val Pro Glu Asn Gln Asn Leu Ile Ser Asn Ile Lys Glu Met
50     55     60
Ile Thr Glu Ala Ser Phe Tyr Leu Phe Asn Ala Thr Lys Arg Arg Val
65     70     75     80
Phe Phe Arg Asn Ile Lys Ile Leu Ile Pro Ala Thr Trp Lys Ala Asn
85     90     95
Asn Asn Ser Lys Ile Lys Gln Glu Ser Tyr Glu Lys Ala Asn Val Ile
100    105    110
Val Thr Asp Trp Tyr Gly Ala His Gly Asp Asp Pro Tyr Thr Leu Gln
115    120    125
Tyr Arg Gly Cys Gly Lys Glu Gly Lys Tyr Ile His Phe Thr Pro Asn
130    135    140
Phe Leu Leu Asn Asp Asn Leu Thr Ala Gly Tyr Gly Ser Arg Gly Arg
145    150    155    160
Val Phe Val His Glu Trp Ala His Leu Arg Trp Gly Val Phe Asp Glu
165    170    175
Tyr Asn Asn Asp Lys Pro Phe Tyr Ile Asn Gly Gln Asn Gln Ile Lys
180    185    190
Val Thr Arg Cys Ser Ser Asp Ile Thr Gly Ile Phe Val Cys Glu Lys
195    200    205
Gly Pro Cys Pro Gln Glu Asn Cys Ile Ile Ser Lys Leu Phe Lys Glu
210    215    220
Gly Cys Thr Phe Ile Tyr Asn Ser Thr Gln Asn Ala Thr Ala Ser Ile
225    230    235    240
Met Phe Met Gln Ser Leu Ser Ser Val Val Glu Phe Cys Asn Ala Ser
245    250    255
Thr His Asn Gln Glu Ala Pro Asn Leu Gln Asn Gln Met Cys Ser Leu
260    265    270
Arg Ser Ala Trp Asp Val Ile Thr Asp Ser Ala Asp Phe His His Ser
275    280    285
Phe Pro Met Asn Gly Thr Glu Leu Pro Pro Pro Pro Thr Phe Ser Leu
290    295    300

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Val Glu Ala Gly Asp Lys Val Val Cys Leu Val Leu Asp Val Ser Ser
305          310          315          320
Lys Met Ala Glu Ala Asp Arg Leu Leu Gln Leu Gln Gln Ala Ala Glu
          325          330          335
Phe Tyr Leu Met Gln Ile Val Glu Ile His Thr Phe Val Gly Ile Ala
          340          345          350
Ser Phe Asp Ser Lys Gly Glu Ile Arg Ala Gln Leu His Gln Ile Asn
          355          360          365
Ser Asn Asp Asp Arg Lys Leu Leu Val Ser Tyr Leu Pro Thr Thr Val
          370          375          380
Ser Ala Lys Thr Asp Ile Ser Ile Cys Ser Gly Leu Lys Lys Gly Phe
385          390          395          400
Glu Val Val Glu Lys Leu Asn Gly Lys Ala Tyr Gly Ser Val Met Ile
          405          410          415
Leu Val Thr Ser Gly Asp Asp Lys Leu Leu Gly Asn Cys Leu Pro Thr
          420          425          430
Val Leu Ser Ser Gly Ser Thr Ile His Ser Ile Ala Leu Gly Ser Ser
          435          440          445
Ala Ala Pro Asn Leu Glu Glu Leu Ser Arg Leu Thr Gly Gly Leu Lys
          450          455          460
Phe Phe Val Pro Asp Ile Ser Asn Ser Asn Ser Met Ile Asp Ala Phe
465          470          475          480
Ser Arg Ile Ser Ser Gly Thr Gly Asp Ile Phe Gln Gln His Ile Gln
          485          490          495
Leu Glu Ser Thr Gly Glu Asn Val Lys Pro His His Gln Leu Lys Asn
          500          505          510
Thr Val Thr Val Asp Asn Thr Val Gly Asn Asp Thr Met Phe Leu Val
          515          520          525
Thr Trp Gln Ala Ser Gly Pro Pro Glu Ile Ile Leu Phe Asp Pro Asp
          530          535          540
Gly Arg Lys Tyr Tyr Thr Asn Asn Phe Ile Thr Asn Leu Thr Phe Arg
545          550          555          560
Thr Ala Ser Leu Trp Ile Pro Gly Thr Ala Lys Pro Gly His Trp Thr
          565          570          575
Tyr Thr Leu Asn Asn Thr His His Ser Leu Gln Ala Leu Lys Val Thr
          580          585          590
Val Thr Ser Arg Ala Ser Asn Ser Ala Val Pro Pro Ala Thr Val Glu
          595          600          605
Ala Phe Val Glu Arg Asp Ser Leu His Phe Pro His Pro Val Met Ile
          610          615          620
Tyr Ala Asn Val Lys Gln Gly Phe Tyr Pro Ile Leu Asn Ala Thr Val
625          630          635          640
Thr Ala Thr Val Glu Pro Glu Thr Gly Asp Pro Val Thr Leu Arg Leu
          645          650          655
Leu Asp Asp Gly Ala Gly Ala Asp Val Ile Lys Asn Asp Gly Ile Tyr
          660          665          670
Ser Arg Tyr Phe Phe Ser Phe Ala Ala Asn Gly Arg Tyr Ser Leu Lys
          675          680          685
Val His Val Asn His Ser Pro Ser Ile Ser Thr Pro Ala His Ser Ile
          690          695          700
Pro Gly Ser His Ala Met Tyr Val Pro Gly Tyr Thr Ala Asn Gly Asn
705          710          715          720
Ile Gln Met Asn Ala Pro Arg Lys Ser Val Gly Arg Asn Glu Glu Glu
          725          730          735
Arg Lys Trp Gly Phe Ser Arg Val Ser Ser Gly Gly Ser Phe Ser Val

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Leu	Gly	Val	Pro	Ala	Gly	Pro	His	Pro	Asp	Val	Phe	Pro	Pro	Cys	Lys
		755						760				765			
Ile	Ile	Asp	Leu	Glu	Ala	Val	Lys	Val	Glu	Glu	Glu	Leu	Thr	Leu	Ser
		770					775				780				
Trp	Thr	Ala	Pro	Gly	Glu	Asp	Phe	Asp	Gln	Gly	Gln	Ala	Thr	Ser	Tyr
785					790					795					800
Glu	Ile	Arg	Met	Ser	Lys	Ser	Leu	Gln	Asn	Ile	Gln	Asp	Asp	Phe	Asn
				805					810					815	
Asn	Ala	Ile	Leu	Val	Asn	Thr	Ser	Lys	Arg	Asn	Pro	Gln	Gln	Ala	Gly
				820				825					830		
Ile	Arg	Glu	Ile	Phe	Thr	Phe	Ser	Pro	Gln	Ile	Ser	Thr	Asn	Gly	Pro
		835					840					845			
Glu	His	Gln	Pro	Asn	Gly	Glu	Thr	His	Glu	Ser	His	Arg	Ile	Tyr	Val
		850				855					860				
Ala	Ile	Arg	Ala	Met	Asp	Arg	Asn	Ser	Leu	Gln	Ser	Ala	Val	Ser	Asn
865					870					875					880
Ile	Ala	Gln	Ala	Pro	Leu	Phe	Ile	Pro	Pro	Asn	Ser	Asp	Pro	Val	Pro
				885					890					895	
Ala	Arg	Asp	Tyr	Leu	Ile	Leu	Lys	Gly	Val	Leu	Thr	Ala	Met	Gly	Leu
			900					905					910		
Ile	Gly	Ile	Ile	Cys	Leu	Ile	Ile	Val	Val	Thr	His	His	Thr	Leu	Ser
		915					920					925			
Arg	Lys	Lys	Arg	Ala	Asp	Lys	Lys	Glu	Asn	Gly	Thr	Lys	Leu	Leu	
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<210> 162
<211> 498
<212> DNA
<213> Homo sapien
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<400> 162						
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<210> 163
<211> 1128
<212> DNA
<213> Homo sapien
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<400> 163							
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atcagctcct	ccatgacaag	gggaagctcca	cccaagatgt	acggcgacga	ttctctcttc		300
accatctgat	cgcagaaatt	ccacacgctg	aaatcagagc	tacctcggag	gtgtccctca		360
actccaagcc	ctctcccaac	acaaaagaacc	aaatccgtccg	attctgggtct	gatgatgaag		420

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<210> 164
 <211> 1310
 <212> DNA
 <213> Homo sapien

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<400> 164
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gatatacata tcaagtatgt tgataaatga cacaatgaag tgtctctatt ttgtgggtga 1200
ttttaatgaa tgcctaaata taattatcca aattgatttt cctttgtgcc cgtaaaaata 1260
acagtatttt aaatttgtaa agaattgtcta ataaaatata atctaattac 1310

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<210> 165
 <211> 177
 <212> PRT
 <213> Homo sapien

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<400> 165
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Ser Tyr Ala Val Pro Ser Cys Gly Arg Ser Val Glu Gly Leu Ser Arg
20          25          30
Arg Leu Lys Arg Ala Val Ser Glu His Gln Leu Leu His Asp Lys Gly
35          40          45
Lys Ser Ile Gln Asp Leu Arg Arg Arg Phe Phe Leu His His Leu Ile

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50		55		60
Ala Glu Ile His Thr	Ala Glu Ile Arg	Ala Thr Ser Glu Val Ser Pro		
65	70	75	80	
Asn Ser Lys Pro Ser	Pro Asn Thr Lys	Asn His Pro Val Arg Phe Gly		
	85	90	95	
Ser Asp Asp Glu Gly Arg Tyr Leu Thr	Gln Glu Thr Asn Lys Val Glu			
	100	105	110	
Thr Tyr Lys Glu Gln Pro Leu Lys Thr	Pro Gly Lys Lys Lys Lys Gly			
	115	120	125	
Lys Pro Gly Lys Arg Lys Glu Gln Glu Lys Lys Lys Arg Arg Thr Arg				
	130	135	140	
Ser Ala Trp Leu Asp Ser Gly Val Thr Gly Ser Gly Leu Glu Gly Asp				
145	150	155	160	
His Leu Ser Asp Thr Ser Thr Thr Ser Leu Glu Leu Asp Ser Arg Arg				
	165	170	175	

His

<210> 166
 <211> 177
 <212> PRT
 <213> Homo sapien

<400> 166
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20 25 30
Arg Leu Lys Arg Ala Val Ser Glu His Gln Leu Leu His Asp Lys Gly
35 40 45
Lys Ser Ile Gln Asp Leu Arg Arg Arg Phe Phe Leu His His Leu Ile
50 55 60
Ala Glu Ile His Thr Ala Glu Ile Arg Ala Thr Ser Glu Val Ser Pro
65 70 75 80
Asn Ser Lys Pro Ser Pro Asn Thr Lys Asn His Pro Val Arg Phe Gly
85 90 95
Ser Asp Asp Glu Gly Arg Tyr Leu Thr Gln Glu Thr Asn Lys Val Glu
100 105 110
Thr Tyr Lys Glu Gln Pro Leu Lys Thr Pro Gly Lys Lys Lys Gly
115 120 125
Lys Pro Gly Lys Arg Lys Glu Gln Glu Lys Lys Lys Arg Arg Thr Arg
130 135 140
Ser Ala Trp Leu Asp Ser Gly Val Thr Gly Ser Gly Leu Glu Gly Asp
145 150 155 160
His Leu Ser Asp Thr Ser Thr Thr Ser Leu Glu Leu Asp Ser Arg Arg
165 170 175

His

<210> 167
 <211> 3362
 <212> DNA
 <213> Homo sapien

<400> 167

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gctcattgca	attaatcctc	aggtacctga	gaatcagaac	ctcatctcaa	acattaaggga	240
aatgataact	gaagcttcat	tttacctatt	taatgctacc	aagagaagag	tatttttcag	300
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agaatcatat	gaaaaaggca	atgtcatagt	gactgactgg	tatggggcac	atggagatga	420
tccatacacc	ctacaataca	gaggggtgtg	aaaagaggga	aaatacattc	atttcacacc	480
taatttccta	ctgaatgata	acttaacagc	tggctacgga	tcacgaggcc	gagtgtttgt	540
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 tt 3362

<210> 168
 <211> 2784
 <212> DNA
 <213> Homo sapien

<400> 168
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 taccaagaga agagtatttt tcagaaatat aaagatttta atacctgcca catggaaaagc 360
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2784

<210> 169
 <211> 592
 <212> PRT
 <213> Homo sapien

<400> 169

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Thr	Leu	Leu	Val	Ala	Leu	Ser	Ser	Glu	Leu	Pro	Phe	Leu	Gly	Ala	Gly
			20					25					30		
Val	Gln	Leu	Gln	Asp	Asn	Gly	Tyr	Asn	Gly	Leu	Leu	Ile	Ala	Ile	Asn
		35				40						45			
Pro	Gln	Val	Pro	Glu	Asn	Gln	Asn	Leu	Ile	Ser	Asn	Ile	Lys	Glu	Met
	50					55					60				
Ile	Thr	Glu	Ala	Ser	Phe	Tyr	Leu	Phe	Asn	Ala	Thr	Lys	Arg	Arg	Val
65					70					75					80
Phe	Phe	Arg	Asn	Ile	Lys	Ile	Leu	Ile	Pro	Ala	Thr	Trp	Lys	Ala	Asn
			85						90					95	
Asn	Asn	Ser	Lys	Ile	Lys	Gln	Glu	Ser	Tyr	Glu	Lys	Ala	Asn	Val	Ile
			100					105					110		
Val	Thr	Asp	Trp	Tyr	Gly	Ala	His	Gly	Asp	Asp	Pro	Tyr	Thr	Leu	Gln
	115				120							125			
Tyr	Arg	Gly	Cys	Gly	Lys	Glu	Gly	Lys	Tyr	Ile	His	Phe	Thr	Pro	Asn
	130				135						140				
Phe	Leu	Leu	Asn	Asp	Asn	Leu	Thr	Ala	Gly	Tyr	Gly	Ser	Arg	Gly	Arg
145					150					155					160
Val	Phe	Val	His	Glu	Trp	Ala	His	Leu	Arg	Trp	Gly	Val	Phe	Asp	Glu
			165						170					175	
Tyr	Asn	Asn	Asp	Lys	Pro	Phe	Tyr	Ile	Asn	Gly	Gln	Asn	Gln	Ile	Lys
			180					185					190		
Val	Thr	Arg	Cys	Ser	Ser	Asp	Ile	Thr	Gly	Ile	Phe	Val	Cys	Glu	Lys
	195					200						205			
Gly	Pro	Cys	Pro	Gln	Glu	Asn	Cys	Ile	Ile	Ser	Lys	Leu	Phe	Lys	Glu
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Gly	Cys	Thr	Phe	Ile	Tyr	Asn	Ser	Thr	Gln	Asn	Ala	Thr	Ala	Ser	Ile
225					230					235					240
Met	Phe	Met	Gln	Ser	Leu	Ser	Ser	Val	Val	Glu	Phe	Cys	Asn	Ala	Ser
			245						250					255	
Thr	His	Asn	Gln	Glu	Ala	Pro	Asn	Leu	Gln	Asn	Gln	Met	Cys	Ser	Leu
			260					265					270		
Arg	Ser	Ala	Trp	Asp	Val	Ile	Thr	Asp	Ser	Ala	Asp	Phe	His	His	Ser
	275						280					285			
Phe	Pro	Met	Asn	Gly	Thr	Glu	Leu	Pro	Pro	Pro	Pro	Thr	Phe	Ser	Leu
	290					295					300				
Val	Glu	Ala	Gly	Asp	Lys	Val	Val	Cys	Leu	Val	Leu	Asp	Val	Ser	Ser
305					310					315					320
Lys	Met	Ala	Glu	Ala	Asp	Arg	Leu	Leu	Gln	Leu	Gln	Gln	Ala	Ala	Glu
			325						330					335	
Phe	Tyr	Leu	Met	Gln	Ile	Val	Glu	Ile	His	Thr	Phe	Val	Gly	Ile	Ala
			340					345					350		
Ser	Phe	Asp	Ser	Lys	Gly	Glu	Ile	Arg	Ala	Gln	Leu	His	Gln	Ile	Asn
	355					360						365			
Ser	Asn	Asp	Asp	Arg	Lys	Leu	Leu	Val	Ser	Tyr	Leu	Pro	Thr	Thr	Val

370 375 380
 Ser Ala Lys Thr Asp Ile Ser Ile Cys Ser Gly Leu Lys Lys Gly Phe
 385 390 395 400
 Glu Val Val Glu Lys Leu Asn Gly Lys Ala Tyr Gly Ser Val Met Ile
 405 410 415
 Leu Val Thr Ser Gly Asp Asp Lys Leu Gly Asn Cys Leu Pro Thr
 420 425 430
 Val Leu Ser Ser Gly Ser Thr Ile His Ser Ile Ala Leu Gly Ser Ser
 435 440 445
 Ala Ala Pro Asn Leu Glu Glu Leu Ser Arg Leu Thr Gly Gly Leu Lys
 450 455 460
 Phe Phe Val Pro Asp Ile Ser Asn Ser Asn Ser Met Ile Asp Ala Phe
 465 470 475 480
 Ser Arg Ile Ser Ser Gly Thr Gly Asp Ile Phe Gln Gln His Ile Gln
 485 490 495
 Leu Glu Ser Thr Gly Glu Asn Val Lys Pro His His Gln Leu Lys Asn
 500 505 510
 Thr Val Thr Val Asp Asn Thr Val Gly Asn Asp Thr Met Phe Leu Val
 515 520 525
 Thr Trp Gln Ala Ser Gly Pro Pro Glu Ile Ile Leu Phe Asp Pro Asp
 530 535 540
 Gly Arg Lys Tyr Tyr Thr Asn Asn Phe Ile Thr Asn Leu Thr Phe Arg
 545 550 555 560
 Thr Ala Ser Leu Trp Ile Pro Gly Thr Ala Lys Pro Gly His Trp Thr
 565 570 575
 Tyr Thr Leu Met Cys Phe His His Ala Lys Leu Leu Thr Trp Lys Leu
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<210> 170
 <211> 791
 <212> PRT
 <213> Homo sapien

<400> 170
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 35 40 45
 Pro Gln Val Pro Glu Asn Gln Asn Leu Ile Ser Asn Ile Lys Glu Met
 50 55 60
 Ile Thr Glu Ala Ser Phe Tyr Leu Phe Asn Ala Thr Lys Arg Arg Val
 65 70 75 80
 Phe Phe Arg Asn Ile Lys Ile Leu Ile Pro Ala Thr Trp Lys Ala Asn
 85 90 95
 Asn Asn Ser Lys Ile Lys Gln Glu Ser Tyr Glu Lys Ala Asn Val Ile
 100 105 110
 Val Thr Asp Trp Tyr Gly Ala His Gly Asp Asp Pro Tyr Thr Leu Gln
 115 120 125
 Tyr Arg Gly Cys Gly Lys Glu Gly Lys Tyr Ile His Phe Thr Pro Asn
 130 135 140
 Phe Leu Leu Asn Asp Asn Leu Thr Ala Gly Tyr Gly Ser Arg Gly Arg
 145 150 155 160
 Val Phe Val His Glu Trp Ala His Leu Arg Trp Gly Val Phe Asp Glu

165 170 175
 Tyr Asn Asn Asp Lys Pro Phe Tyr Ile Asn Gly Gln Asn Gln Ile Lys
 180 185 190
 Val Thr Arg Cys Ser Ser Asp Ile Thr Gly Ile Phe Val Cys Glu Lys
 195 200 205
 Gly Pro Cys Pro Gln Glu Asn Cys Ile Ile Ser Lys Leu Phe Lys Glu
 210 215 220
 Gly Cys Thr Phe Ile Tyr Asn Ser Thr Gln Asn Ala Thr Ala Ser Ile
 225 230 235 240
 Met Phe Met Gln Ser Leu Ser Ser Val Val Glu Phe Cys Asn Ala Ser
 245 250 255
 Thr His Asn Gln Glu Ala Pro Asn Leu Gln Asn Gln Met Cys Ser Leu
 260 265 270
 Arg Ser Ala Trp Asp Val Ile Thr Asp Ser Ala Asp Phe His His Ser
 275 280 285
 Phe Pro Met Asn Gly Thr Glu Leu Pro Pro Pro Thr Phe Ser Leu
 290 295 300
 Val Glu Ala Gly Asp Lys Val Val Cys Leu Val Leu Asp Val Ser Ser
 305 310 315 320
 Lys Met Ala Glu Ala Asp Arg Leu Leu Gln Leu Gln Gln Ala Ala Glu
 325 330 335
 Phe Tyr Leu Met Gln Ile Val Glu Ile His Thr Phe Val Gly Ile Ala
 340 345 350
 Ser Phe Asp Ser Lys Gly Glu Ile Arg Ala Gln Leu His Gln Ile Asn
 355 360 365
 Ser Asn Asp Asp Arg Lys Leu Leu Val Ser Tyr Leu Pro Thr Thr Val
 370 375 380
 Ser Ala Lys Thr Asp Ile Ser Ile Cys Ser Gly Leu Lys Lys Gly Phe
 385 390 395 400
 Glu Val Val Glu Lys Leu Asn Gly Lys Ala Tyr Gly Ser Val Met Ile
 405 410 415
 Leu Val Thr Ser Gly Asp Asp Lys Leu Leu Gly Asn Cys Leu Pro Thr
 420 425 430
 Val Leu Ser Ser Gly Ser Thr Ile His Ser Ile Ala Leu Gly Ser Ser
 435 440 445
 Ala Ala Pro Asn Leu Glu Glu Leu Ser Arg Leu Thr Gly Gly Leu Lys
 450 455 460
 Phe Phe Val Pro Asp Ile Ser Asn Ser Asn Ser Met Ile Asp Ala Phe
 465 470 475 480
 Ser Arg Ile Ser Ser Gly Thr Gly Asp Ile Phe Gln Gln His Ile Gln
 485 490 495
 Leu Glu Ser Thr Gly Glu Asn Val Lys Pro His His Gln Leu Lys Asn
 500 505 510
 Thr Val Thr Val Asp Asn Thr Val Gly Asn Asp Thr Met Phe Leu Val
 515 520 525
 Thr Trp Gln Ala Ser Gly Pro Pro Glu Ile Ile Leu Phe Asp Pro Asp
 530 535 540
 Gly Arg Lys Tyr Tyr Thr Asn Asn Phe Ile Thr Asn Leu Thr Phe Arg
 545 550 555 560
 Thr Ala Ser Leu Trp Ile Pro Gly Thr Ala Lys Pro Gly His Trp Thr
 565 570 575
 Tyr Thr Leu Asn Asn Thr His His Ser Leu Gln Ala Leu Lys Val Thr
 580 585 590
 Val Thr Ser Arg Ala Ser Asn Ser Ala Val Pro Pro Ala Thr Val Glu
 595 600 605

Ala Phe Val Glu Arg Asp Ser Leu His Phe Pro His Pro Val Met Ile
 610 615 620
 Tyr Ala Asn Val Lys Gln Gly Phe Tyr Pro Ile Leu Asn Ala Thr Val
 625 630 635 640
 Thr Ala Thr Val Glu Pro Glu Thr Gly Asp Pro Val Thr Leu Arg Leu
 645 650 655
 Leu Asp Asp Gly Ala Gly Ala Asp Val Ile Lys Asn Asp Gly Ile Tyr
 660 665 670
 Ser Arg Tyr Phe Phe Ser Phe Ala Ala Asn Gly Arg Tyr Ser Leu Lys
 675 680 685
 Val His Val Asn His Ser Pro Ser Ile Ser Thr Pro Ala His Ser Ile
 690 695 700
 Pro Gly Ser His Ala Met Tyr Val Pro Gly Tyr Thr Ala Asn Gly Asn
 705 710 715 720
 Ile Gln Met Asn Ala Pro Arg Lys Ser Val Gly Arg Asn Glu Glu Glu
 725 730 735
 Arg Lys Trp Gly Phe Ser Arg Val Ser Ser Gly Gly Ser Phe Ser Val
 740 745 750
 Leu Gly Val Pro Ala Gly Pro His Pro Asp Val Phe Pro Pro Cys Lys
 755 760 765
 Ile Ile Asp Leu Glu Ala Val Asn Arg Arg Gly Ile Asp Pro Ile Leu
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 Asp Ser Thr Trp Arg Arg Leu
 785 790

<210> 171
 <211> 1491
 <212> DNA
 <213> Homo sapien

<400> 171
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 tgagaaggtt tctctcacat ctagaagaa ggccttaaga tgtggcagcc cctctctctc 180
 aagtggctct tgcctgttg cctgggagt tctcaaattg ctgcagcagc ctcacccag 240
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 gactctcctg ggcgaccccg agagcttacc attcctcaga cttcttcaca tgggtgtaac 360
 agatttgttc ctaaaagtaa agctctagag gccgtcaaat tggcaataga agccgggttc 420
 caccatattg attctgcaca tgtttacaat aatgaggagc aggttggact ggccatccga 480
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 caattggact atgttgacct ctatcttatt cattttccag tgtctgtaaa gccagggtgag 660
 gaagtgatcc caaaagatga aaatggaaaa atactatttg acacagtggg tctctgtgcc 720
 acatgggagg ccatggagaa gtgtaaagat gcaggattgg ccaagtcctat cgggggtgtcc 780
 aacttcaacc acaggctgct ggagatgac ctcaacaagc cagggtctca gtacaagcct 840
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 aagtcacaaag acattgttct ggttgcttat agtgctctgg gatcccatcg agaagaacca 960
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 gtcttgccca agagctacaa tgagcagcgc atcagacaga acgtgcaggt gtttgaattc 1140
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 ctatgctggg gactggacac atgcctctg gtaaatctc tcttgcttgg cgacttcagt 1380
 aagctacagc taagcccatc ggccgaaaaa gaaagacaat aattttgttc ttcattttga 1440

aaaaattaaa tgctctctcc taaagattct tcacctaaaa aaaaaaaaaa a

1491

<210> 172
 <211> 364
 <212> PRT
 <213> Homo sapien

<400> 172
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 Ser Ser Gln Ile Ala Ala Ala Ser Thr Gln Pro Glu Asp Asp Ile
 20 25 30
 Asn Thr Gln Arg Lys Lys Ser Gln Glu Lys Met Arg Glu Val Thr Asp
 35 40 45
 Ser Pro Gly Arg Pro Arg Glu Leu Thr Ile Pro Gln Thr Ser Ser His
 50 55 60
 Gly Ala Asn Arg Phe Val Pro Lys Ser Lys Ala Leu Glu Ala Val Lys
 65 70 75 80
 Leu Ala Ile Glu Ala Gly Phe His His Ile Asp Ser Ala His Val Tyr
 85 90 95
 Asn Asn Glu Glu Gln Val Gly Leu Ala Ile Arg Ser Lys Ile Ala Asp
 100 105 110
 Gly Ser Val Lys Arg Glu Asp Ile Phe Tyr Thr Ser Lys Leu Trp Ser
 115 120 125
 Asn Ser His Arg Pro Glu Leu Val Arg Pro Ala Leu Glu Arg Ser Leu
 130 135 140
 Lys Asn Leu Gln Leu Asp Tyr Val Asp Leu Tyr Leu Ile His Phe Pro
 145 150 155 160
 Val Ser Val Lys Pro Gly Glu Glu Val Ile Pro Lys Asp Glu Asn Gly
 165 170 175
 Lys Ile Leu Phe Asp Thr Val Asp Leu Cys Ala Thr Trp Glu Ala Met
 180 185 190
 Glu Lys Cys Lys Asp Ala Gly Leu Ala Lys Ser Ile Gly Val Ser Asn
 195 200 205
 Phe Asn His Arg Leu Leu Glu Met Ile Leu Asn Lys Pro Gly Leu Lys
 210 215 220
 Tyr Lys Pro Val Cys Asn Gln Val Glu Cys His Pro Tyr Phe Asn Gln
 225 230 235 240
 Arg Lys Leu Leu Asp Phe Cys Lys Ser Lys Asp Ile Val Leu Val Ala
 245 250 255
 Tyr Ser Ala Leu Gly Ser His Arg Glu Glu Pro Trp Val Asp Pro Asn
 260 265 270
 Ser Pro Val Leu Leu Glu Asp Pro Val Leu Cys Ala Leu Ala Lys Lys
 275 280 285
 His Lys Arg Thr Pro Ala Leu Ile Ala Leu Arg Tyr Gln Leu Gln Arg
 290 295 300
 Gly Val Val Val Leu Ala Lys Ser Tyr Asn Glu Gln Arg Ile Arg Gln
 305 310 315 320
 Asn Val Gln Val Phe Glu Phe Gln Leu Thr Ser Glu Glu Met Lys Ala
 325 330 335
 Ile Asp Gly Leu Asn Arg Asn Val Arg Tyr Leu Thr Leu Asp Ile Phe
 340 345 350
 Ala Gly Pro Pro Asn Tyr Pro Phe Ser Asp Glu Tyr
 355 360